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**AIR POLLUTION: AIR QUALITY CRITERIA FOR
NITROGEN OXIDES**

**NATO Committee on the Challenges of Modern
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AIR QUALITY CRITERIA FOR NITROGEN OXIDES

A Report by the Expert Panel

on

Air Quality Criteria

COMMITTEE ON THE CHALLENGES OF MODERN SOCIETY

NORTH ATLANTIC TREATY ORGANIZATION

JUNE 1973

ia

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FOREWORD

The material presented in this document represents an effort by the Expert Panel on Air Quality Criteria, Committee on the Challenges of Modern Society, NATO, to compile a compendium of information using the United States Air Quality Criteria for Nitrogen Oxides as a basic document on the effects of nitrogen oxides (NO_x) in the ambient air on man and his environment. Nitric oxide (NO) and nitrogen dioxide (NO_2), the nitrogen oxides that are primarily considered in this report, are collectively referred to herein as NO_x .

Air quality criteria are an expression of the scientific knowledge of the relationship between various concentrations of pollutants in the air and their adverse effects on man and his environment. Air quality criteria are descriptive; that is, they describe the effects that have been observed to occur when the concentration of a pollutant in the ambient air has reached or exceeded a specific level for a specific time period. In the development of criteria, many factors, including exposure time and conditions of the environment, must be considered. The criteria must also include consideration of the contributions of all such variables to the effects of air pollution on human health, agriculture, materials, visibility, and climate. Further, the individual characteristics of the receptor must be taken into account.

This document focuses on nitrogen oxides as found in the ambient air; therefore, literature on extremely high levels of (NO_x) has not been extensively cited. The occurrence, properties, and fate of atmospheric NO_x and the principles of formation and control are reviewed

in the earlier chapters; these are followed by a discussion of measurement methods and chemical interactions of atmospheric NO_x . The effects of NO_x are considered in relation to materials, vegetation, animals, and man. Reviews of both toxicological and epidemiological studies are presented. It should be noted that the reference conditions for converting units of pollutant concentration are 25°C and 760 mm Hg.

Recent interest and activity on the part of the public, governmental, scientific, academic, and industrial sectors of our communities have stimulated research on the effects of pollution on man and his environment. The result is an ever-increasing body of knowledge that must be analyzed, interpreted, and finally expressed as information supporting or refuting suggested criteria. The assimilation of this new knowledge is not a task that can be undertaken by a small body of men--such as a committee of this nature. Rather, the responsibility for ensuring that criteria continually reflect the most significant information available rests with those same sectors of our communities that have inspired all of us to strive to improve our environment--the public, the government, the scientific, the academic, and the industrial sectors.

The Panel encourages and welcomes new data, comments, and constructive criticism of this document. We suggest that a procedure be established whereby this document and documents to follow can be revised and updated periodically.

For the Expert Panel,

F. G. Hueter, Ph.D., Chairman

ACKNOWLEDGMENT

The Chairman of the Expert Panel on Air Quality Criteria wishes to acknowledge the scientists participating from pilot, co-pilot, and observer countries and the many other persons who assisted in the preparation of this document.

The working group, which performed diligently through the course of this effort, receives the highest praise. The group members were:

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In particular, special thanks are due the Environmental Protection Agency of the United States for permission to use their document. Air Quality Criteria for Nitrogen Oxides, which was published in 1971, as a base for our effort.

Full recognition is given to each panel member for carrying out and coordinating review and other activities related to the development of this document in his respective country, to Dr. I. J. Buurma of the National Institute of Public Health of the Netherlands for his effort as host for the working meeting, to Mr. H. W. Goerke of the Ministry of the Interior of the Federal Republic of Germany for his assistance in arranging the working meeting, to Dr. David Shearer, Dr. David Coffin, and Mr. Rudolph Boksleitner for preparation of this document, and to staff members of the Technical Publications Branch, Office of Administration, U. S. Environmental Protection Agency, Research Triangle Park, North Carolina, for editorial work.

Finally, acknowledgment must be given to Mrs. Kathryn L. Dunn, who typed this entire document, and to those other secretaries and other personnel who have assisted in bringing the panel effort to fruition.

F. G. Hueter, Ph.D.

Panel Chairman

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CHAPTER 1.

PROPERTIES OF NITROGEN OXIDES AND PHYSICAL EFFECTS ON LIGHT TRANSMISSION

A. INTRODUCTION

Of the various oxides of nitrogen, the most important as air pollutants are nitric oxide (NO) and nitrogen dioxide (NO₂). Other known oxides of nitrogen include nitrous oxide (N₂O), nitrogen sesquioxide (N₂O₃), nitrogen tetroxide (N₂O₄), and nitrogen pentoxide (N₂O₅); but, of these four, only N₂O is present in the atmosphere in appreciable concentrations.

The term NO_x is used to represent the composite atmospheric concentration of nitric oxide and nitrogen dioxide throughout this document.

B. OCCURRENCE

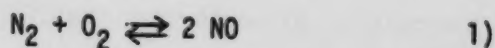
Nitric oxide and a comparatively small amount of NO₂ are formed under high-temperature conditions such as those that accompany the burning of fossil fuels. The pollutants are emitted to the atmosphere from automobile exhausts, furnace stacks, incinerators, and vents from certain chemical processes. Although vast quantities are produced by natural biological reactions, the resultant concentrations of atmospheric NO_x are low because these reactions take place over wide areas. Most of the NO_x produced technologically is in the form of NO, which is subsequently oxidized in the atmosphere to the more toxic and irritant NO₂. Normally, at low NO concentrations of 1.2 mg/m³ (1 ppm) or less, the direct reaction with oxygen in the air proceeds slowly. The oxidation of NO to NO₂ is speeded up enormously, however, by photochemical processes involving reactive hydrocarbons.

Nitrous oxide (N_2O) is not considered an air contaminant, and no evidence exists to suggest that N_2O is involved in photochemical reactions in the lower atmosphere. Formation of N_2O largely results from the decomposition of nitrogen compounds by soil bacteria and from reactions between nitrogen and atomic oxygen or ozone in the upper atmosphere (1). The mean atmospheric concentration of N_2O is about $449 \mu\text{g}/\text{m}^3$ (0.25 ppm) (2). The oxides, N_2O_4 , N_2O_3 , and N_2O_5 , are not found in appreciable concentrations under urban atmospheric conditions. Nevertheless, it is feasible that even in small concentrations N_2O_3 and N_2O_5 could be involved in reactions that lead to photochemical air pollution (3).

C. PROPERTIES OF NITROGEN OXIDES

1. Nitric Oxide (NO)

Nitric oxide, a colorless, odorless gas, which is slightly soluble in water, is the primary product formed during high-temperature combustion processes when atmospheric oxygen and nitrogen combine according to the following endothermic reaction:

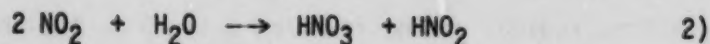


This reaction continues to an equilibrium level, dependent upon variables such as the temperature of the flame, the concentration of each gas, and the movement of the gases through different zones of temperatures, pressures, and concentrations. When rapid cooling follows combustion, time is inadequate for equilibrium to develop, and nitric oxide persists in the flame products.

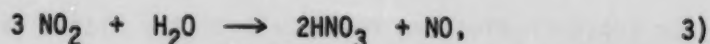
2. Nitrogen Dioxide (NO_2)

Nitrogen dioxide is a reddish-orange-brown gas with a characteristic pungent odor. Although its boiling point is 21.2°C , the low partial

pressure of NO_2 in the atmosphere restricts it to the gas phase at normal atmospheric temperatures. Nitrogen dioxide is corrosive and highly oxidizing, and may be physiologically irritating and toxic. Although NO_2 reacts with water to form nitric acid and either nitrous acid or NO :



or



the reaction of NO_2 with H_2O has not been shown to have any significance in polluted air (3).

Although NO_2 exists in equilibrium with its dimer, nitrogen tetroxide (N_2O_4):



the fraction present in dimer form is negligible at atmospheric concentrations of NO_2 .

NO_2 is a product of the reaction of nitric oxide with oxygen as described in the following equation:



The feature of this reaction is that the reaction rate decreases as temperature increases. The above reaction should not be considered a termolecular reaction but rather one that involves the following two distinct steps:



The formation of the dimer N_2O_2 is an exothermic reaction because a new bond is formed. Therefore, an increase in temperature will decrease

the concentrations of N_2O_2 , which decreases the rate of reaction and the amount of NO_2 formed.

Nitric oxide can be converted to NO_2 by other reaction mechanisms such as a chain reaction where the oxygen atoms are simply the initiators of the chain, or a free radical chain reaction with NO as the chain carrier (4). Because the rate of oxidation of NO depends on the first power of the oxygen concentration and the square of the nitric oxide concentration, the rate of mixture or dilution must be very slow in order to permit a significant oxidation of the nitric oxide to the thermodynamically favored nitrogen dioxide. In the case of automobile exhaust, the dilution rate is too rapid to permit such oxidation and therefore nitric oxide predominates over nitrogen dioxide.

The conversion of NO to NO_2 in air is greatly accelerated by the simultaneous presence of hydrocarbons and exposure to sunlight. It is apparent that this conversion is related to the oxidation of the hydrocarbons.

It is possible to explain NO_2 formation by an alternative mechanism. Nitrogen dioxide formation may result from reaction of O_2 with the dimer of the NO molecule:



At present, it is not possible to prove which of the proposed schemes more correctly describes the mechanism of NO_2 formation in the atmosphere.

During daylight hours, atmospheric NO may be quantitatively converted to NO_2 by reactions that involve absorption of sunlight energy by NO_2 and subsequent interaction with certain hydrocarbons and oxygen.

A detailed description of the nitrogen dioxide photolytic cycle and photochemical interaction with hydrocarbons is given in references 5 and 6.

Schematically, the NO_2 photolytic cycle has the form shown in Figure 1-1. The wavelengths of light responsible for NO_2 photolysis are the ultraviolet portions of sunlight energy reaching the earth's surface, i.e., 3000 to 4000 Å. The NO_2 absorption spectrum is shown in Figure 1-2. Wavelengths longer than 4000 Å are efficiently absorbed by

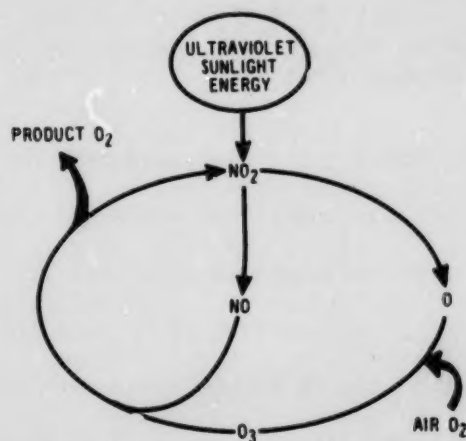


Figure 1-1. Atmospheric NO_2 photolytic cycle.

NO_2 , but such absorption does not add sufficient energy to break bonds. Ultraviolet absorption, on the other hand, adds enough energy to break one of the N-O bonds in the NO_2 molecule. The dissociation energy of the ON-O bond, 71.7 kcal/mole, is equivalent to the light wavelength of 4000 Å. The released oxygen atom reacts rapidly with atmospheric oxygen to form ozone, which in turn, reacts rapidly with the NO formed in the breakup of the NO_2 molecule. The result in the atmosphere is the rapid cycling of the NO_2 . With the possible exception of minor secondary reactions, Figure 1-1 describes the NO_2 photolytic cycle. If there were no

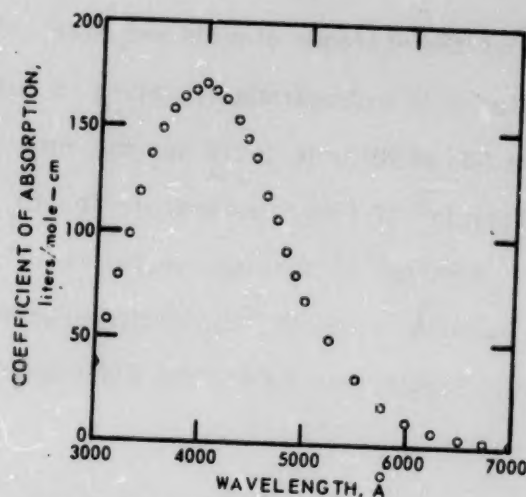


Figure 1-2. NO_2 absorption spectrum (developed from reference 3).

competing reactions, the photolytic cycle would have no overall net effect; that is, ambient NO and NO_2 concentrations would not change as a result of NO_2 photolysis. The same pollutant sources that emit NO_x , however, also emit hydrocarbons (HC). Interaction of HC with the NO_2 photolytic cycle increases the speed of the NO to NO_2 conversion and thus unbalances the cycle in favor of NO_2 formation. This is discussed in greater detail in Chapter 5.

3. Nitrous Oxide (N_2O)

Nitrous oxide, a colorless and odorless gas used as an anesthetic, is familiarly known as "laughing gas". Nitrous oxide is present in the atmosphere (about 0.25 ppm), but is chemically inert at normal atmospheric temperatures and is, therefore, not considered an air pollutant. It may be a minor product of the atmospheric interactions of NO_2 in the presence of hydrocarbons and sunlight.

4. Nitrogen Tetroxide (N_2O_4)

Nitrogen tetroxide is the colorless dimer of nitrogen dioxide. Its

formation is favored by high NO_2 concentrations. At the dilute NO_2 concentrations found in ambient atmospheres, however, N_2O_4 cannot be present in more than trace amounts and therefore is probably of minor importance in atmospheric reactions.

5. Nitrogen Pentoxide (N_2O_5)

Nitrogen pentoxide may be an intermediate in atmospheric reactions (3). It can be found in the reaction between nitrogen dioxide and ozone.

6. Other Oxides of Nitrogen

Nitrogen trioxide (NO_3) is thought to be an important intermediate in atmospheric reactions, but equilibrium and reaction kinetics factors do not favor accumulation of significant (or measurable) levels. Both NO_3 and N_2O_2 have been suggested as intermediates during the formation of NO_2 when NO reacts with O_2 . Nitrogen sesquioxide (N_2O_3) may be an intermediate in atmospheric reactions (3).

A summary of the physical properties of the oxides of nitrogen is presented in Table 1-1.

D. EFFECTS ON ATMOSPHERIC LIGHT TRANSMISSION

Visibility reduction, one of the most common manifestations of urban air pollution, is caused by the scattering and absorption of light by particles or gases in the atmosphere and depends in a complicated way on the concentration and properties of the gases and particles present (see reference 8).

Nitrogen dioxide is intensely colored and absorbs light over the entire visible spectrum, but primarily in the shorter wavelengths, violet, blue, and green. In the atmosphere NO_2 reduces the brightness and contrast of distant objects and causes the horizon sky and white objects

Table 1-1. PHYSICAL PROPERTIES OF NITROGEN OXIDES (7)

Oxide	Molecular weight	Melting point, °C	Boiling point, °C	Density, g/liter	Specific gravity ^a
NO	30.01	-163.6	-151.8	1.3204	--
NO ₂	46.01	-11.2	21.2	--	1.4494 ²⁰ ₂₀
N ₂ O	44.01	-90.8	-88.5	1.977	--
N ₂ O ₃	76.01	-102	3.5 ^b	--	1.477 ²
N ₂ O ₄	92.02	c	c	c	c
N ₂ O ₅	108.01	30	47 ^b	--	1.642 ¹⁸

^aSuperscript: temperature of liquid, °C, Subscript: temperature of water, °C.

^bDecomposes.

^cValue uncertain, dimer of NO₂.

to appear pale yellow to reddish-brown. A token amount of light is attenuated by the molecular scattering effect of NO₂.

Figure 1-3 shows the calculated percent of visible light transmitted as a function of wavelength for different atmospheric NO₂ concentrations and viewing distances in an aerosol-free atmosphere. Each curve is based on the concentration (ppm)-distance (mile) product; thus, 3 ppm-mile could be 1 ppm at 3 miles, or 3 ppm at 1 mile, or any combination of concentration and distance whose product is 3. A more normal picture of conditions actually existing in the atmosphere, with both NO₂ and aerosols present, is shown in Figure 1-4. These data are given in terms of calculated attenuation coefficients (9). Here, the effect of

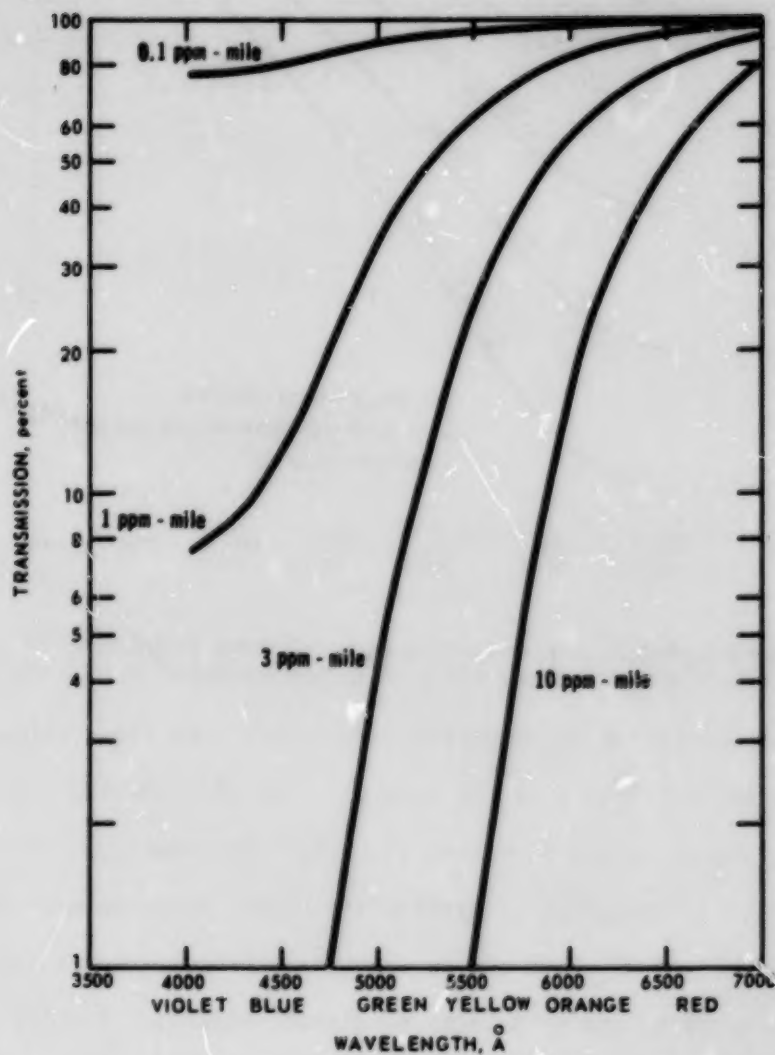


Figure 1-3. Transmittance of visible light at different NO₂ concentrations and viewing distances (9).

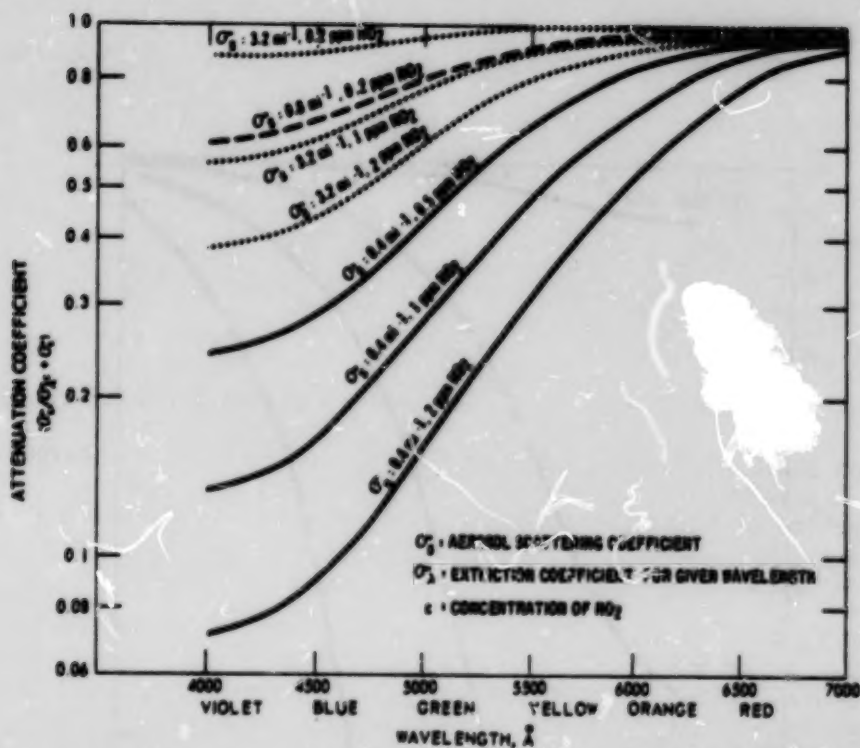


Figure 1-4. Aerosol attenuation in spectral luminance of horizon sky and distant objects at different NO_2 and aerosol concentrations.

visible light absorption is accompanied by transmitted light attenuation because of light scattering by the aerosol. The photochemical system involves NO_x and HC in the formation of visibility-reducing aerosols.

The additional presence of particulate matter tends to mask the coloration effect of NO_2 , but the two combined markedly reduce the visibility, contrast, and brightness of distant objects. Particulate matter and aerosols are present in the atmosphere as primary contaminants from urban sources such as industrial combustion and vehicular transportation, and from natural sources such as the sea, soil, and fog. These contaminants are also formed through photochemical reactions and are considered to be the major cause of the reduced visibility associated with photochemical smog.

Light scattering associated with the presence of aerosols is the primary cause of visibility reduction in photochemical smog; absorption of light by NO_2 makes a minor contribution.

E. SUMMARY

As used here, the term NO_x represents the sum of NO and NO_2 , the only significant nitrogen oxide air pollutants. The major oxide in combustion emissions is NO . The rapid cooling of the gases in the combustion chamber prevents dissociation back to nitrogen and oxygen. A small fraction of NO is converted to NO_2 by reaction with oxygen during the exhaust dilution process; however, the major pathway leading to formation of NO_2 from NO is the photochemical interaction between NO_x and hydrocarbons.

Nitrogen dioxide causes reduction of visibility and coloration of the horizon sky in degrees dependent on the concentration of the pollutant, the viewing distance, and the accompanying aerosol concentration. The presence of photochemical aerosol or other particulate matter suppresses the coloration effect of NO_x and increases the visibility-reduction effect.

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CHAPTER 2.

SOURCES AND CONTROL OF ATMOSPHERIC NITROGEN OXIDES

A. INTRODUCTION

The major component of worldwide atmospheric nitrogen oxides (NO_x) is biologically produced nitric oxide (NO) (1). Natural sources produce about 450 million metric tons (MT) (500 million tons*) of NO per year; man-made sources emit 45 million MT (50 million tons) per year of NO_x , which includes NO and nitrogen dioxide (NO_2).

In general, NO_x concentrations in urban atmospheres are 10 to 100 times higher than those in nonurban atmospheres. Problems associated with NO_x consequently reflect the importance of technological sources over natural sources. Recent estimates indicate that total emission rates of NO_x from man-made sources in the United States have increased from approximately 15 million MT (17 million tons) in 1966 to 21 million MT (23 million tons) in 1970 (2), nearly 50 percent of the world production.

B. MAN-MADE SOURCES

Fuel combustion is the major cause of technology-associated NO_x emissions. In 1970 coal, oil, natural gas, and motor-vehicle fuel combustion accounted for over 19.7 (21.9) out of an estimated 20.5 million MT (22.8 million tons) of man-made NO_x in the United States. Of the 9 million MT (10 million tons) generated by stationary combustion sources, power plants emitted 2.9 million MT (3.2 million tons); industries 4.3 million MT (4.8 million tons); and home and office heating plants, the remaining 1.8 million MT (2 million tons). Natural-gas-burning sources made the largest contribution of any fuel

*2000 pounds per ton

in the stationary source group. With many small- and medium-size combustion units the absolute emission was found to be dependent on the type of fuel and to decrease in the order coal > oil > gas (3-5).

An estimated 10.5 million MT (11.7 million tons) was emitted from transportation sources in the United States, 8.2 million MT (9.1 million tons) of which was from motor vehicles. Industrial processes, solid waste disposal, and other miscellaneous sources accounted for about 2.3 million MT (2.5 million tons) of NO_x . The distribution of NO_x emissions by major source categories is indicated in Table 2-1.

Relatively small quantities of NO_x are emitted from noncombustion industrial processes, mainly those that manufacture or use nitric acid (6). Even though total quantities may be small, high concentrations of NO_x can be emitted from some of these chemical processes. Electroplating, engraving, welding, metal cleaning, and detonating explosives can be responsible for industrial NO_x emissions, as can the manufacture and use of liquid- NO_x -based rocket propellants.

In the United States over 60 percent of the total NO_x emissions occur in highly populated areas; 60 percent of stationary source emissions and 45 percent of motor-vehicle emissions occur in urban areas (2). The emissions from a single stack of a nitric-acid-producing plant can amount to 0.40 to 0.46 MT (0.44 to 0.51 tons) of NO_x per hour (7).

The proportion of nitrogen oxide emissions from various sources in France is shown in Table 2-2. Table 2-3 contains estimated emissions of NO_x from stationary sources for several European and North American countries and for Japan for the years 1968 and 1980 (9).

Table 2-1. SUMMARY OF NITROGEN OXIDES EMISSIONS IN UNITED STATES, 1970 (2)

Source category	Emissions	
	10 ⁶ metric tons/year	percent
Transportation	10.6	51.3
Motor vehicles	8.3	39.9
Gasoline	7.1	34.2
Diesel	1.2	5.7
Aircraft ^a	0.4	1.8
Railroads	0.1	0.4
Vessels	0.2	0.9
Nonhighway	1.7	8.3
Fuel combustion in stationary sources	9.1	43.8
Coal	3.5	17.1
Fuel oil	1.2	5.7
Natural gas ^b	4.3	20.6
Wood	0.1	0.4
Industrial processes	0.2	0.9
Solid waste disposal	0.4	1.8
Miscellaneous	0.5	2.2
Forest fires	0.2	0.9
Structural fires	N ^c	N
Coal refuse	N	N
Agricultural	0.3	1.3
	20.8	100.0

^aEmissions below 900m (3000 ft).

^bIncludes liquified petroleum gas (LPG) and kerosene.

^cN = Negligible.

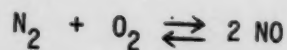
Table 2-2. NITROGEN OXIDE EMISSIONS IN FRANCE, 1970 (8)

Source	Percent of total emissions
Motor vehicles	40
Domestic power production	23
Industrial power production	18
Petroleum industry	10
Domestic heating	8
Miscellaneous	1
	100

C. PRINCIPLES OF FORMATION AND CONTROL

1. Formation

Nitric oxide is formed during fossil-fuel combustion according to the reaction:



The equilibrium level depends upon such variables as flame temperature, pressure, concentration of each gas, retention time in zones of different temperatures, and rates of cooling. The NO, which is formed, can react with more oxygen to form NO₂. Equilibrium concentrations of the NO_x mixture constituents are a function of the variables encountered during combustion and the subsequent extraction of heat from the gases. The formation of NO and the achievement of equilibrium is favored by high temperatures; whereas, oxidation to NO_x is an exothermic, second-order reaction favored by lower temperatures. Consequently, high combustion temperatures, rapid cooling, and instantaneous dilution of exhaust gases

Table 2-3. ESTIMATED TOTAL EMISSION OF NITROGEN OXIDES FROM
STATIONARY SOURCES, 1968 AND 1980 (NO SPECIAL ABATEMENT
MEASURES IN 1980) (9)

Country	NO _x , 10 ⁶ metric tons	
	1968	1980
Finland	0.119	0.208
Sweden	0.103	0.224
Norway	0.027	0.038
Denmark	0.088	0.148
Total	0.337	0.618
United Kingdom	1.065	1.19
The Netherlands	0.220	0.374
Germany	1.26 ^a	1.94 ^a
Belgium	0.177	0.232
France	0.494	0.588
Total	3.216	4.324
Switzerland	0.035	0.054
Austria	0.078	0.098
Total	0.113	0.152
Spain	0.210	0.518
Italy	0.418	1.124
Greece	0.035	0.116
Turkey	0.137	0.317
Total	0.800	2.075
United States	9.02	16.01
Canada	0.31	0.59
Total	9.33	16.60
Japan	0.97	3.36
Grand total	14.8	27.1

^aMean of range.

promote the emission of high concentrations of NO and low concentrations of NO₂. The peak temperatures in an internal combustion piston engine are extremely high and cause high concentrations of NO_x.

Another parameter that influences the exhaust-gas composition is the ratio of the mixed air and fuel. Maximum NO concentration occurs with 5 to 10 percent excess air. The curve of NO concentration as a function of the relative air-fuel ratio, calculated for chemical equilibrium at the end of the combustion cycle is shown in Figure 2-1. The NO-forming reactions are completed before reaching the equilibrium concentrations of Figure 2-1. The actual NO concentrations of the exhaust gases are thus much lower as shown in Figure 2-2. Recent studies show that such reactions

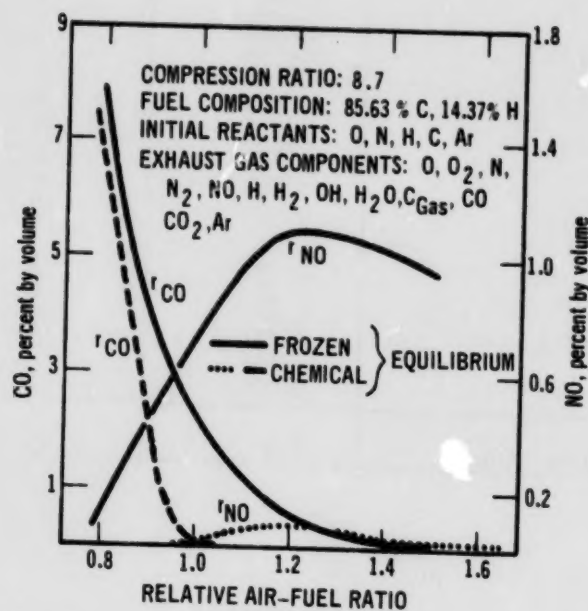


Figure 2-1. Effect of relative air-fuel ratio on exhaust gas CO and NO concentrations considering the ideal Otto cycle (r_{CO} = percent by volume of CO; r_{NO} = percent by volume of NO in the exhaust gas)(10).

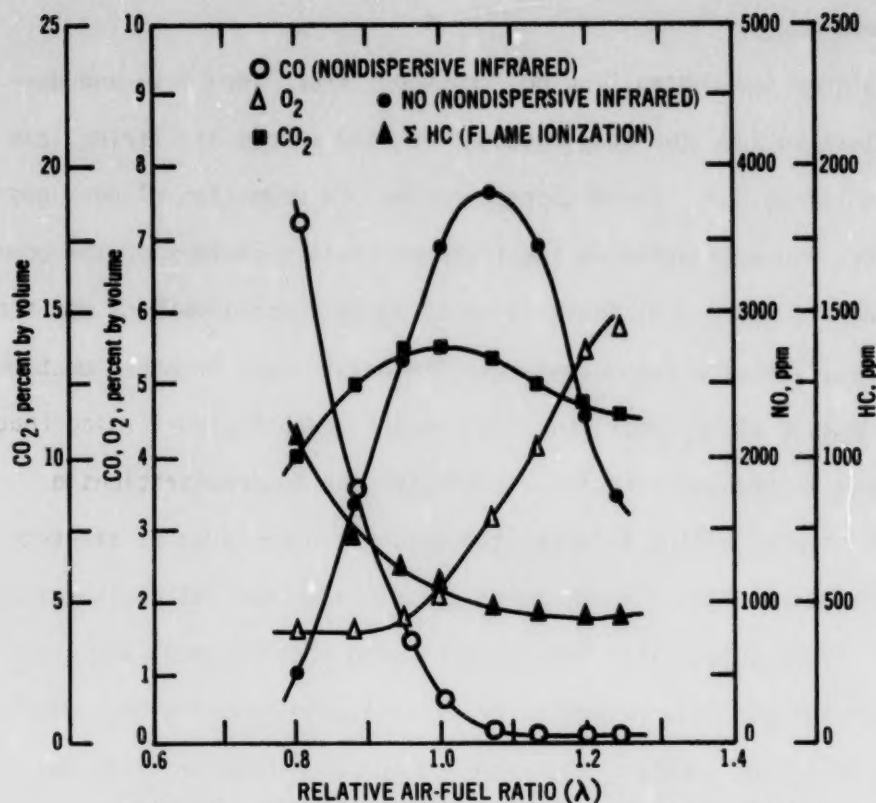


Figure 2-2. Exhaust gas composition of a 6-cylinder, fuel-injected Otto engine as a function of the relative air-fuel ratio (λ). (λ = actual air to stoichiometric air ratio. $1\lambda = 14.7$ kg air/kg fuel.) Engine data: compression ratio, 8.7; throttle position, 80°; rpm, 3600; displacement, 2195 cc (11).

in the cylinder of internal combustion engines are detectable by using spectroscopic equipment (12). The steep slope of the NO concentration in the region of excess air in Figure 2-2 relative to Figure 2-1 reflects poor combustion conditions. Additional information concerning NO_x emissions from vehicular engines may be found in references 12 through 17.

An excellent review of the formation of NO_x upon combustion of coal has been prepared by Dumoutet et al. (18).

2. Control

Techniques for controlling NO_x emissions from large oil- and gas-fired boilers include two-stage combustion, low-excess-air firing, and furnace modifications. These approaches involve reduction of peak gas temperatures and alteration in the time-temperature history of the combustion gases. Commercial feasibility of these control methods has been demonstrated; research is now under way to adapt these or other methods to the reduction of NO_x emissions from coal-fired boilers.

Control techniques directed at reducing the temperature in the combustion chamber of the internal combustion engine--such as exhaust-gas recirculation, higher-than-stoichiometric air-fuel ratios, water injection, spark retardation during high-speed acceleration, and low compression ratios--have proved to be effective in reducing NO_x emissions. It should be noted, however, that some of these methods may lead to increased HC and CO emissions as the NO_x is reduced.

Catalytic methods have been used to control NO_x emissions from chemical process industries, notably nitric acid manufacturing. One of the major problems is the reduction of catalyst life because of contamination by other chemical compounds. Caustic scrubbing, another control technique, is employed in the chemical industries; other techniques are under active investigation. Control of emissions from stationary sources is described in reference 19.

Catalytic control approaches that are applicable to motor-vehicle-exhaust emissions are the subject of extensive research by catalyst manufacturers and the motor vehicle industry. The simultaneous control of NO, CO, and HC is a complex, interrelated problem. One approach to

NO_x emission control involves the catalytic reaction of CO with NO to form elemental nitrogen and carbon dioxide. This approach, however, is complicated by current motor-vehicle-exhaust control methods aimed at the elimination of CO.

More elaborate discussion of the technology applicable to control of emissions from mobile sources is presented in reference 20.

D. SUMMARY

The quantity of NO_x generated by natural sources greatly exceeds the man-made quantity on a worldwide basis. Man's contribution is a cause for concern, however, because the emissions are concentrated in urban areas. Fuel combustion for transportation, power, and heating is the major source of man-made NO_x air pollution. Chemical processing is responsible for high, but localized, emissions.

Control of nitrogen oxide emissions has been directed at both combustion sources and chemical processes. For stationary combustion sources, the control principle has been based on reducing either the flame temperature or the availability of oxygen, both of which prevent NO formation. Similar principles of control are applicable to motor vehicles. Catalytic principles, which have been applied to reduce NO_x from chemical processes, may also be applicable to the control of NO_x in motor-vehicle exhaust.

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CHAPTER 3.

METHODS FOR MEASUREMENT OF NITROGEN OXIDES

A. INTRODUCTION

The most accurate, reliable, and useful methods for the measurement of atmospheric nitric oxide (NO), nitrogen dioxide (NO₂), and nitrogen oxides (NO_x) employ standard techniques to collect the samples in an absorbing solution. The analytical determination is made colorimetrically or spectrophotometrically. Analytical methods based on physical properties such as absorption or emission of radiation, those based on gas-chromatographic separation and detection, and those based on oxidation or reduction are not in common use but will probably receive more attention in the future. Measurement techniques for other oxides of nitrogen will not be discussed in this chapter.

B. NITROGEN DIOXIDE

1. Manual Methods

a. Griess-Saltzman Method

The colorimetric Griess-Saltzman method (1,2) is the most suitable manual method generally applicable to the measurement of NO₂ in the atmosphere. This method is based on the reaction of NO₂ with sulfanilic acid, to form a diazonium salt that couples with N-(1-naphthyl)-ethylenediamine dihydrochloride to produce a deeply colored azodye.

Air is sampled through a fritted bubbler into a solution of the Griess-Saltzman reagent for periods of 30 minutes or less, and the

color is allowed to develop for an additional 15 minutes after completion of sampling. The color produced, which is proportional to the amount of NO_2 sampled, is measured at 550 nanometers (nm). The method can be used to determine concentrations of NO_2 in the air from 40 to $1500 \mu\text{g}/\text{m}^3$ (0.02 to 0.80 ppm). Kothny and Mueller (3) have indicated sulfanilamide has an advantage over sulfanilic acid in that the diazotation reaction proceeds faster.

Ordinarily, interferences are not a problem, although high ratios of sulfur dioxide to nitrogen dioxide (about 30:1) can cause bleaching and give misleadingly low values (1). Interference from other oxides of nitrogen or ozone are negligible at concentrations found in polluted air. Peroxyacetylnitrate (PAN) can give a response of up to 35 percent of an equivalent molar concentration of NO_2 , but in ordinary ambient air PAN concentrations are too low to cause significant error (1). The color formed is reasonably stable, but samples should be read within 1 hour of completion of sampling.

In the original method, Saltzman (4) used solutions of sodium nitrite as calibration standards. He reported that, under laboratory conditions, 0.72 mole of nitrite produces the same color as 1 mole of NO_2 gas and incorporated this factor into his calculations. In recent years this stoichiometric factor has been the source of considerable controversy. Values ranging from 0.5 to 1.00 have been reported (5-11), and one recent study (12) reconfirmed Saltzman's original findings. Studies in France (13) have indicated that this factor is 0.77. The method can be standardized

by using an accurately determined concentration of NO_2 gas and thus eliminate the stoichiometric factor from the calculations.

b. Other Manual Methods

The unmodified Griess-Saltzman method for NO_2 measurement cannot be used successfully when the delay between sample collection and color measurement is more than 4 to 6 hours or when sampling periods of longer than 1 hour are required. In such situations the Jacobs-Hochheiser method (14) has been used. In this method, however, the absorption efficiency for NO_2 varies with the sampling system used and the ambient concentration (15). Various collection efficiencies have been reported (16, 17, 18). Hauser and Shy (15) have presented additional information on the inherent deficiencies in the Jacobs-Hochheiser procedure.

Other investigators have reported on other manual methods for NO_2 measurement (19-21). These are currently being evaluated.

2. Continuous Method

Most continuous NO_2 analyzers use the Griess-Saltzman method or a slight modification of it. The sample air is drawn through an absorber at an accurately determined flow rate countercurrent to a controlled flow of absorbing reagent. The absorber must be carefully designed and properly sized because NO_2 is somewhat difficult to absorb. Sufficient time is allowed for full color development, and then the colored solution is passed to a colorimeter or spectrophotometer where the intensity is measured continuously at 550 nm.

3. Miscellaneous Methods

Correlation spectrometry (22,23), gas chromatography (24), long-path infrared spectroscopy, and electrochemical oxidation and reduction (25) have been applied to NO and NO₂ analysis, but have not found wide application in atmospheric sampling and measurement. Correlation spectrometry, a promising new technique for remote sensing, requires further field trials before it can be adopted for routine air pollution measurement (26). Gas chromatography is potentially a useful and versatile method for measuring NO₂. Long-path infrared spectroscopy uses large-volume cells that make rapid response difficult to achieve in a continuous-monitoring instrument. Long-path infrared also has the disadvantage that water vapor interferes with the measurements. Electrochemical transducers, which operate on the principle of oxidation or reduction of pollutant absorbed on a sensing electrode, show excellent potential as simple, compact means for measuring NO₂ and NO_x in ambient air.

The German Air Quality System uses a continuous coulometric method for the monitoring of NO₂ (27). In Vienna, Austria, long path NO₂ measurement has been carried out by the principle of light absorption in the visible wavelength range (28).

Recently, devices that operate on the principle of chemiluminescence have been developed (29,30). In the first method a detector measures the luminescence produced during the gas-phase reaction between NO and ozone. In the second method, NO_x concentrations are determined indirectly by measuring the equilibrium ozone concentrations under continuous u. v. irradiation. During operation, ambient air flows

continuously through a calibrated orifice into a vessel, where it is mixed with ozone and gives rise to measurable luminescence proportionate to the NO concentration. Part of the same air is passed through a device that converts the NO₂ present into NO; then this air is mixed with ozone to provide a luminescence reading that represents the NO_x (NO plus NO₂) in the air sample. Subtracting the NO from the NO_x concentration provides the NO₂ concentration. This approach represents a promising development in direct NO-measurement methodology.

4. Calibration

Any measurement method should be calibrated to assure accuracy. The procedure for calibrating a method for measuring NO₂ is to use the entire system, including the sampling line and its components, to analyze an atmosphere containing accurately known amounts of NO₂ in the concentration range to be studied. These calibration gases can be generated by simple-gas-dilution with check-analysis (31), by precision-gas-dilution without check-analysis (10), by a gravimetric procedure (32), by an electrolysis system (33), or by use of a permeation tube (34). The permeation tube procedure is by far the most accurate and simplest of these methods. In another less complex procedure for calibration (35), accurately known concentrations of sodium nitrite solutions are used to calibrate the analytical portion of the method. Because the sampling efficiency of the method being calibrated is not taken into account, the procedure is considered inferior to the permeation tube method.

Permeation tubes deserve special mention because of their accuracy, simplicity, and growing use. A permeation tube is a device used to generate artificial atmospheres with known NO₂ concentrations (12).

Constructed of Teflon,* it contains a liquified gas such as NO_2 , which permeates through the walls at a slow but constant rate as long as the temperature of the device is held constant. An improved permeation device was recently reported upon (36). The permeation rate of the gas can be accurately determined (37). One suitable system using a permeation tube is shown schematically in Figure 3-1. The

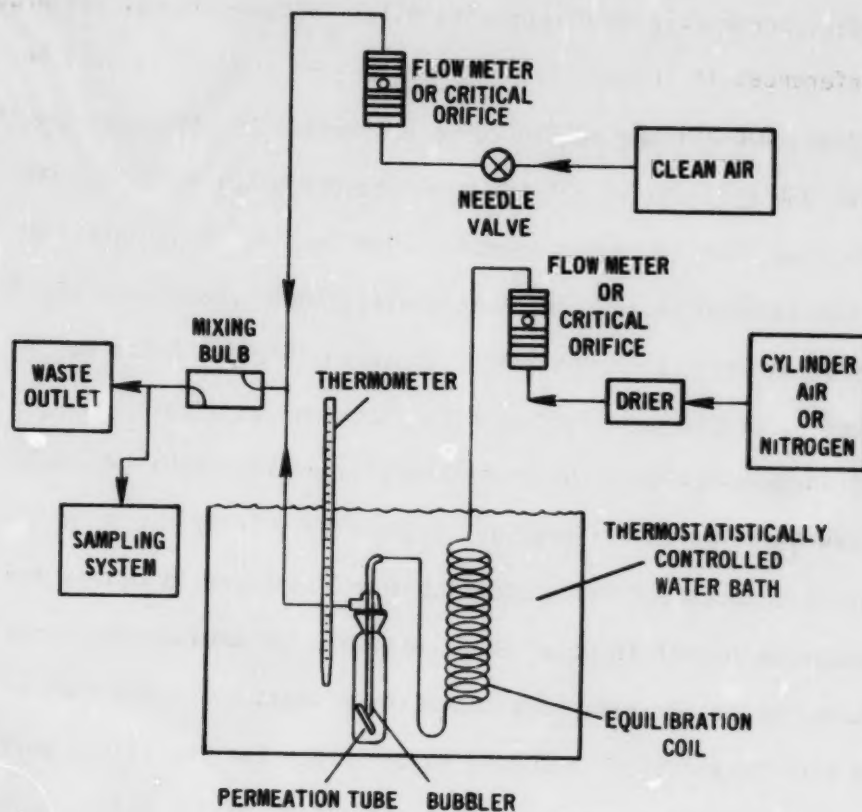


Figure 3-1. Permeation tube system.

*Mention of a specific commercial product or company name does not constitute endorsement.

temperature of the bath containing the permeation device must be held constant, preferably within 0.1 °C, and the air or nitrogen passed across the permeation tube must be dry. This technique has been used for both field and laboratory calibrations. Nitrogen dioxide permeation tubes are moisture-sensitive, and care must be taken to protect them from atmospheric moisture during use and storage.

After any method has been calibrated under closely controlled laboratory conditions, preferably using the permeation tube technique, the problem of interferences in the ambient air at the sampling site should be considered. One method for dealing with the interference problem is to use local ambient air, for which NO₂ background is determined concurrently, as dilution air. Such a procedure will be satisfactory if all of the precautions in the use of permeation tubes, particularly that measure of allowing only dry air or nitrogen to pass over the tube, are observed.

It should be pointed out that permeation tubes constructed of glass tubing with a small segment of Teflon* tubing at one end are better than Teflon* tubes because of the rapid diffusion of NO₂ through Teflon.* It is also important to note that the liquid should be kept out of contact with the permeation device itself particularly during transport.

C. NITRIC OXIDE

1. Oxidation to Nitrogen Dioxide

Nitric oxide is generally determined by oxidizing it to NO₂, measuring the NO₂, and converting the values to NO concentrations. The oxidation step is as yet poorly understood. Some workers find it unreliable and report conversion efficiencies ranging from 40 to 110

percent (35,38). The oxidizers used are aqueous (39) or solid (40) potassium permanganate and dichromate or chromium trioxide in various formulations (38,41,42) all of which have uncertain lifetimes at peak efficiency. In addition, the dichromate and chromium trioxide preparations are extremely sensitive to high humidity. A promising method is one developed by Hartkamp (43).

It is generally believed that NO concentrations are underestimated as a result of the poor conversion efficiency, a factor that should be kept in mind when studying NO data. Steps can be taken to minimize the problem, but oxidation of NO to NO₂ must always be considered a potential source of error.

A new oxidizing reagent with a high collection efficiency (93%) in the concentration range between 250 to 620 $\mu\text{g}/\text{m}^3$ (0.2 to 0.5 ppm) NO has been described by Forwerg and Crecelius (44). The moisture content of the test gas can be reduced by phosphoric acid. This procedure increases the stability of the oxidizer to several weeks.

a. Series Mode

The measurement of NO by the oxidation method can be done in either a series or a parallel mode. In the series mode (Figure 3-2A), which some workers (45,46) prefer, the sample air passes through an NO₂ analyzer for removal and measurement of NO₂, then through an oxidizer where NO is converted to NO₂, and finally through a second NO₂ analyzer. The response from the second NO₂ analyzer is a measure of the NO in the sample air. However up to 14 percent of the NO₂ may be converted to NO in the first analyzer. Therefore it is better to remove the NO₂ by a special absorber, such as triethanolamine on firebrick (47). Even in

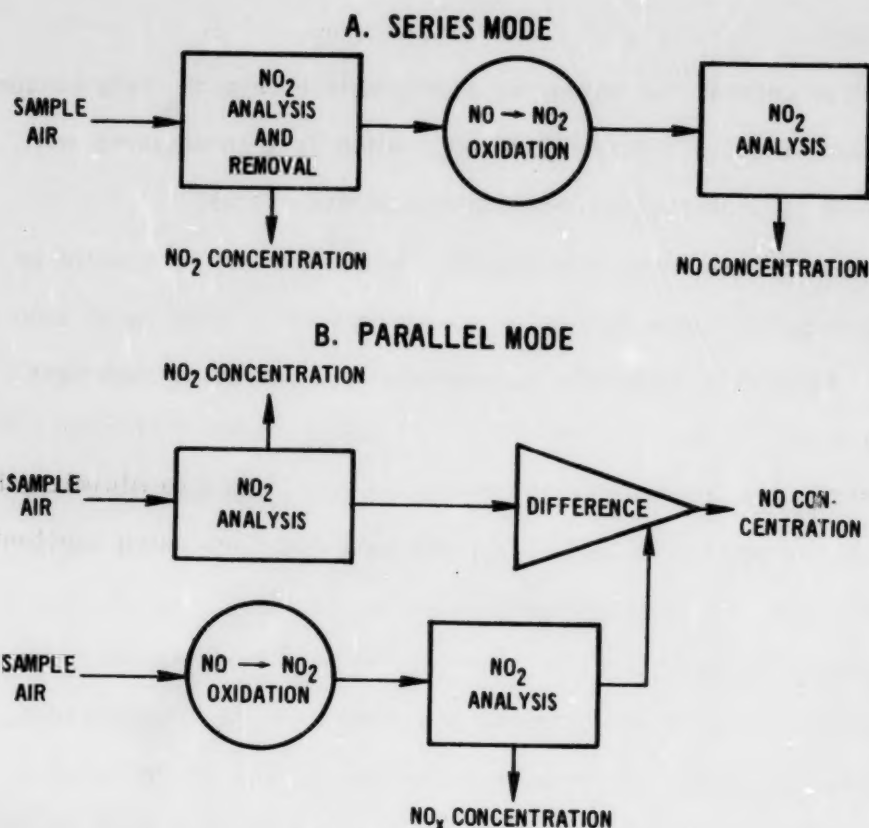


Figure 3-2. Oxidation schemes for analyzing NO and NO_x.

this case up to a few percent of the NO₂ may be converted to NO, depending on the humidity and the age of the absorber.

b. Parallel Mode

The parallel mode (Figure 3-2B), requires two separate analyses. In one, sample air is analyzed for NO₂; and in the other, sample air is analyzed for total NO_x. The NO concentration is the difference between the total NO_x and the value for NO₂. In order to carry out the analysis for total NO_x, the sample air is passed through an oxidizing scrubber to convert NO into NO₂. In addition to the usual problem of uncertain efficiency in NO to NO₂ conversion, the problem of possible capture of NO₂ by the scrubber adds to any basic unreliability in the procedure.

D. SUMMARY

Most procedures for measuring atmospheric NO and NO_x rely on some type of converter to oxidize NO to NO₂, which is then measured and arithmetically converted to respective numerical values.

Any method used for measuring NO₂ in the ambient air should be calibrated before use with sample atmospheres containing known amounts of NO₂. Permeation tubes are recommended for generating such test atmospheres.

For sampling periods of 30 minutes or less, the most suitable method for measuring NO₂ is the manual colorimetric Griess-Saltzman method in which the color developed depends on conversion of NO₂ to nitrite ion. The degree of conversion of NO₂ gas into nitrite ion remains a point of controversy in the Griess-Saltzman and other methods. Nonetheless, this method is relatively free of interferences and may be employed to determine concentrations of NO₂ ranging from 40 to 1500 µg/m³ (0.02 to 0.80 ppm).

For periods of from 30 minutes to 3 hours, sampling can be done either by taking the appropriate number of discrete 30-minute samples with the manual Griess-Saltzman method or by using the continuous Griess-Saltzman method for the entire period.

For sampling periods of 3 to 24 hours or for situations where analysis must be delayed more than 4 hours after sampling, no thoroughly tested method for measuring NO₂ is currently available. The methods described in references 19 through 21 are currently being tested.

For continuous NO₂ measurements, the most suitable method currently available is based on the Griess-Saltzman procedure. When used in

conjunction with an oxidizing scrubber for conversion of NO to NO₂, the continuous Griess-Saltzman method can also be used, in either the series or parallel mode, for measuring NO in ambient air. Researchers disagree as to which of the two modes is more satisfactory, but the major problem with NO measurement lies in completely oxidizing NO to NO₂.

Total nitrogen oxides can be determined by summing NO and NO₂ concentrations from separate samples, or by oxidizing NO to NO₂ and then measuring NO₂.

New approaches for measuring NO and NO_x based on chemiluminescence are promising, but have yet to be adequately field-tested.

Research is still needed to develop and thoroughly evaluate sensitive, reliable, and practical methods for determining NO, NO₂, and NO_x. Considerable standardization, calibration, as well as analytical quality control must be carried out before new methods can be deemed adequate for the collection of reliable data.

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CHAPTER 4.

ATMOSPHERIC LEVELS OF NITROGEN OXIDES

A. INTRODUCTION

The ambient concentration of oxides of nitrogen (NO_x) varies greatly with time and place. Values reported since 1961 appear to have several characteristic concentration patterns. The data, which includes day-mean values for different time periods, have been evaluated in terms of both temporal and meteorological variables because these factors as well as measurement variables must be considered in a complete description of atmospheric levels of NO_x .

B. TEMPORAL VARIATIONS IN NO_x CONCENTRATIONS

1. Natural Sources

On a global basis the major proportion of NO_x is nitric oxide (NO) produced by bacterial action. Relatively little is known about the global circulation of atmospheric NO_x , and only a few data on background concentration of NO_x are available from scattered nonurban areas.

Lodge and Pate (1) found average values of NO_x ranging from $1.8 \mu\text{g}/\text{m}^3$ (0.9 ppb) during the dry season to $7.1 \mu\text{g}/\text{m}^3$ (3.6 ppb) during rainy periods in Panama. Individual samples were as high as $12 \mu\text{g}/\text{m}^3$ (6 ppb). Junge (2) reported NO_2 concentrations averaging $1.8 \mu\text{g}/\text{m}^3$ (0.9 ppb) in Florida and $2.5 \mu\text{g}/\text{m}^3$ (1.3 ppb) in Hawaii.

At Pikes Peak in the Rocky Mountains of Colorado, Hamilton (3) reported an average nitrogen dioxide (NO_2) concentration of $8.0 \mu\text{g}/\text{m}^3$ (4.1 ppb) and an average NO level of $3.3 \mu\text{g}/\text{m}^3$ (2.7 ppb). Ripperton et al. (4) found an average NO_2 concentration of $9.0 \mu\text{g}/\text{m}^3$ (4.6 ppb)

in the Appalachian area of North Carolina. From these data, Robinson and Robbins (5,6) have concluded that North American continental average levels of NO_2 are about $8 \mu\text{g}/\text{m}^3$ (4 ppb) and those of NO are about $2 \mu\text{g}/\text{m}^3$ (2 ppb). They charted a tentative, simplified global nitrogen circulation pattern. Based upon the estimated global background level and the annual emission rates, the average residence time for NO_2 is about 3 days and for NO, about 4 days. Residence times reflect the action of natural scavenging processes including photochemical reactions. In addition, the residence time of NO_2 and NO will be shorter in the more urbanized and polluted areas.

Although scientists tend to emphasize the role of photochemical processes in urban areas, these processes occur during daylight in any area where the ambient air contains NO_x and reactive hydrocarbons.

In remote areas in West Germany, NO_x concentrations ranging from 2 to $5.6 \mu\text{g}/\text{m}^3$ (1 to 3 ppb) seem to represent the natural background level of NO_x (7,8). Measurements taken on mountains and from aircraft indicate that there is a decrease in NO_x concentrations with increasing elevation (9). This seems to hold whether one is in an urban or remote area. In nonurban areas from ground level to heights of about 1000 meters (3280 ft), the NO_x concentration decreases from 9.4 to $3.8 \mu\text{g}/\text{m}^3$ (5 ppb to 2 ppb) of nitrogen dioxide (9).

2. Diurnal Patterns

On a normal day in a city, ambient NO_x levels follow a regular pattern with the sun and traffic. Before daylight, nitric oxide and nitrogen dioxide remain relatively stable at concentrations somewhat higher than the daily minimum. As human activity, especially reflected by

automotive traffic, increases in the hours just after dawn (0600 to 0800 hr), the concentration of the primary contaminant, NO, increases. Then, as ultraviolet energy from the sun becomes available, the NO₂ concentration generally increases until nearly all of the primary NO is converted to secondary NO₂. As the NO concentration approaches low levels (<0.1 ppm), photochemical oxidants begin to accumulate and reach a peak about midday. Concurrent with NO₂ and oxidant formation, both NO and NO₂ become incorporated into products such as the peroxyacyl nitrates and other nitrated compounds.

As solar intensity decreases, atmospheric stability increases, and winds decrease. In urban areas the increased automobile traffic in late afternoon and evening (1700 to 2000 hr) also increases concentrations of primary NO, but solar energy is generally unavailable to convert NO to NO₂ or to cause formation of oxidants. The absence of sunlight, however, does not completely halt NO₂ formation. The principal oxidant present, ozone (O₃), continues to react rapidly with NO to form NO₂ until the O₃ supply is exhausted; thus, the evening NO₂ concentrations may continue to rise. This condition may be ascribed to meteorological factors and, on cold evenings, to increased emissions from stationary sources.

Table 2-1 shows that transportation sources contribute 51 percent of the NO_x emissions in the United States. This table does not account for the spatial distribution of NO_x sources. In the center of major cities, where most air monitoring stations are located, the contribution of mobile sources to NO_x levels may be considerably higher than the reported 51 percent. For this reason, traffic volume, which is highly

variable but easily documented, becomes an important tool in identifying NO_x and relating the pollutant to a recognized emission--automotive exhaust.

The diurnal variations of NO , NO_2 , carbon monoxide (CO), and O_3 in Los Angeles, California, on July 19, 1965, are shown in Figure 4-1. This concentration profile graphically depicts the NO peak and the associated lag in NO_2 peak as the NO is converted. It also illustrates the subsequent increase in O_3 concentration. The data in Figure 4-1 do not show the generalized increase in evening NO_x levels described in the previous paragraph. On this particular day, evening dispersion factors

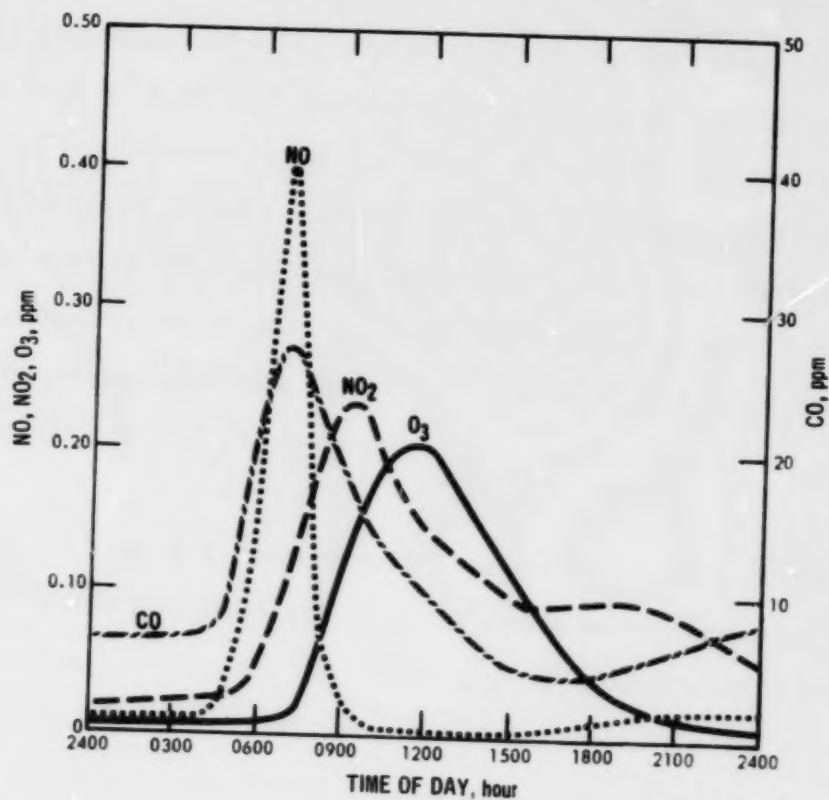


Figure 4-1. Average daily 1-hour concentrations of selected pollutants in Los Angeles, California, July 19, 1965 (10).

apparently prevented any substantial buildup of the NO_x . It should be pointed out that Los Angeles, however, is a unique city because of the tremendous influence of automobile emissions; other cities, around the world, would not necessarily exhibit the same characteristics.

Figures 4-2 through 4-5 depict the diurnal variation of NO_2 in selected cities of Europe and the United States. It should be noted that each graph represents a different averaging time, however, the typical pattern of diurnal NO_2 concentrations is depicted in each figure. Figure 4-2 presents the diurnal variation of NO_2 for 3 different days during May 1971 at a central city site in Rome, Italy. From this figure, it is obvious that the daily NO_2 concentration peaks occur between 0600-0900 hr and 2100-2400 hr. This figure is based on data averaged for 3 hours on individual days. Figure 4-3 presents the diurnal variation of NO_2 based on data collected in Vienna, Austria between April 12 and May 19, 1966. This data was collected hourly by photographing the extinction spectra of a light beam and then determining the concentration based on the density of the photograph. Figure 4-4 shows diurnal variations in NO_2 concentration in several cities in the United States. Sampling was by a continuous Griess-Saltzman method. Plots are based on annual averages of hourly data. Figure 4-5 shows the diurnal variation in NO_2 for three sites in The Netherlands. The plots are based on annual averages.

From Figure 4-6 it can be concluded that the atmospheric NO_2 level is more or less the same for the five weekdays with a somewhat lower concentration on Saturday and Sunday.

The hours at which the peak concentrations of NO_x usually occur either coincide with, or take place shortly after, the hours of peak automotive traffic. The diurnal pattern, therefore, shows little day-

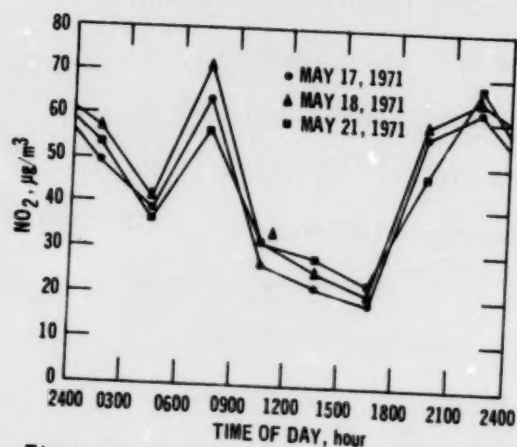


Figure 4-2. Diurnal variation of NO_2 in Rome, Italy, 1971 (11).

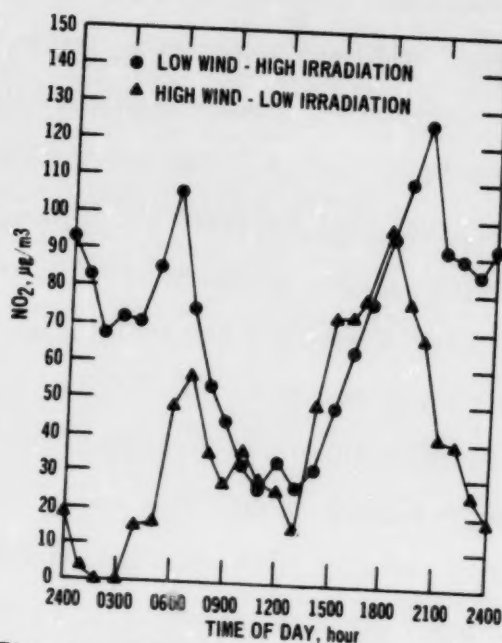


Figure 4-3. Diurnal variation of NO_2 in Vienna, Austria, 1966 (12).

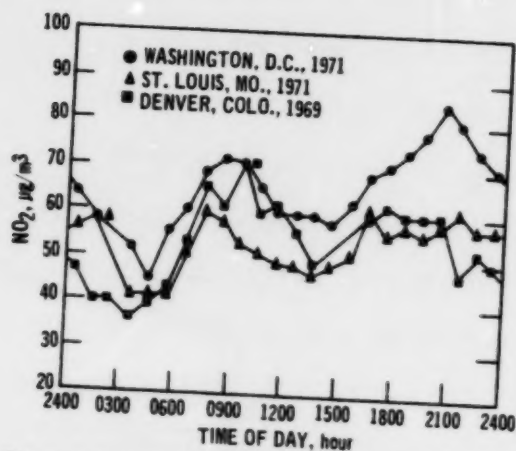


Figure 4-4. Diurnal variation of NO_2 at sites in the United States (13).

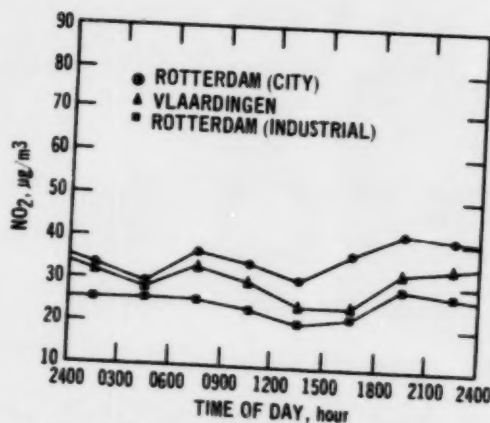


Figure 4-5. Diurnal variation of NO_2 at three sites in The Netherlands, 1971 (14,15).

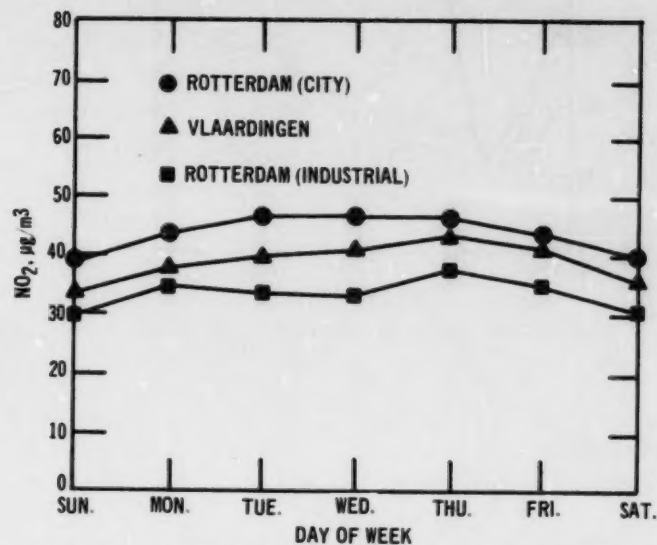


Figure 4-6. Weekly trend in NO_2 concentrations derived from all observations at three sites in The Netherlands, 1970 (14,15).

to-day variation except for weekends and holidays, when traffic differs from weekday patterns. The diurnal variations of NO on weekdays, Saturdays, and Sundays are shown for the Chicago CAMP* station in Figure 4-7. The Sunday peak concentrations of NO at 0800 are about one-third of the weekday peak concentrations. On some weekends, some locations have peak NO concentrations equal to weekday peak values, but the peaks occur 1 to 3 hours later. Furthermore, weekend NO concentrations in certain recreational areas often exceed weekday values.

A recent publication (17) presented the diurnal variation of the NO emissions from automobile traffic in a city of Western Germany for weekdays. This data was the result of an extensive study during the establishment of a general emission register. The influence of the rush-hour to the diurnal variation of the NO_x concentration in the ambient air is supported by these studies (Figure 4-8).

*Continuous Air Monitoring Projects of the U. S. Environmental Protection Agency.

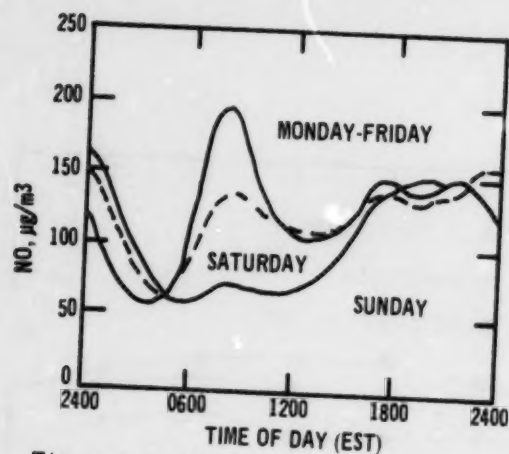


Figure 4-7. Weekday and weekend 1-hour-average NO levels in Chicago, Illinois, 1962 through 1964 (16).

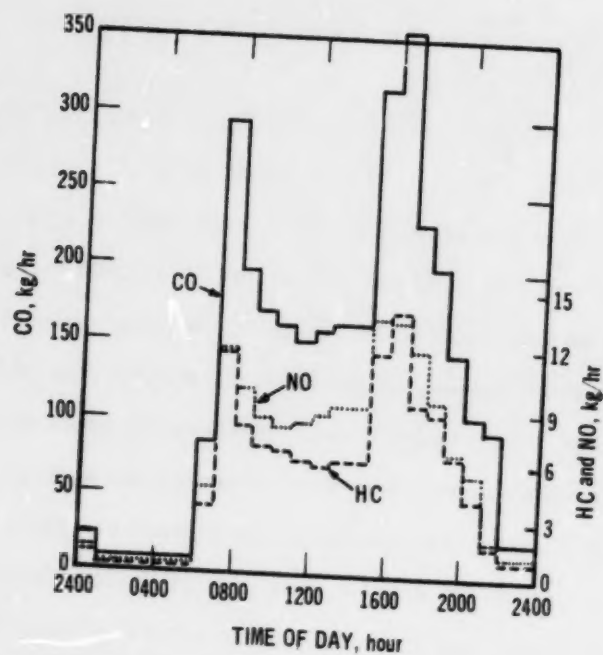


Figure 4-8. Diurnal pattern of vehicle emissions, Monday through Friday, on a freeway in Cologne, West Germany (6 lanes, 5 km) (17).

3. Seasonal Patterns

Nitric oxide displays a more marked seasonal variation than NO_2 does. This can be seen when Figures 4-9 and 4-10 are compared and when Figures 4-11 and 4-12 are compared. For NO , as for most primary contaminants, higher mean values are observed during late fall and through the winter months, when there is less overall atmospheric mixing and generally less ultraviolet energy available for forming secondary products. Measurements in Frankfurt/Main, West Germany show a well defined seasonal pattern for NO_2 with a minimum in the summertime and maxima in autumn and late winter. In this region the NO variation is more pronounced than the NO_2 variation (18).

Figures 4-9 and 4-11 show the seasonal patterns in NO by presenting the mean values by month of the year, during the time period indicated, for Rome, Italy (Figure 4-9); and for the cities of Denver, Colorado, St. Louis, Missouri, and Washington, D. C. (Figure 4-11). The distinctly higher levels during winter are evident.

The pattern for NO_2 (Figures 4-10 and 4-12) is less distinct and shows less variation from month to month.

Figure 4-13 shows the monthly average concentrations measured at three sites in The Netherlands. Fluctuations in concentration over the year are less than for the cities depicted in Figures 4-10 and 4-12.

The high wintertime NO_x values correspond in part to increased NO emissions from power generation and heating sources. Variations in dispersion factors further influence NO_2 and NO_x concentrations.

4. Annual Trends

The ability to determine possible year-to-year trends in air quality depends upon the extent to which cyclical, seasonal, and

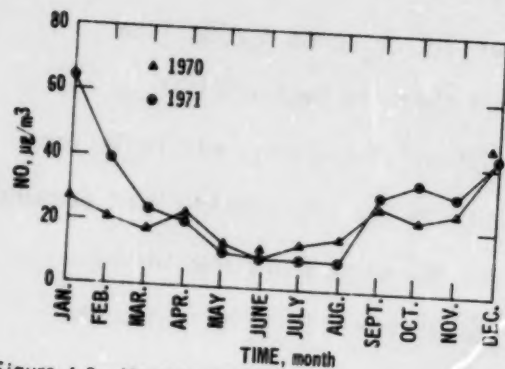


Figure 4-9. Monthly average of NO concentration in Rome, Italy (11).

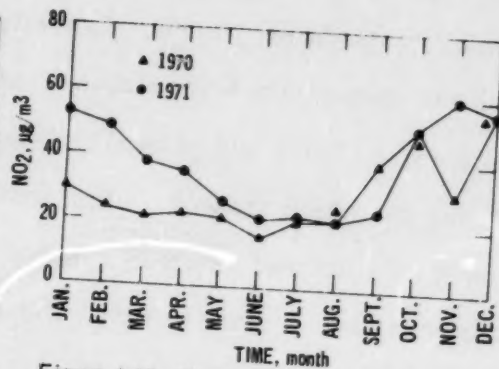


Figure 4-10. Monthly average of NO₂ concentration in Rome, Italy (11).

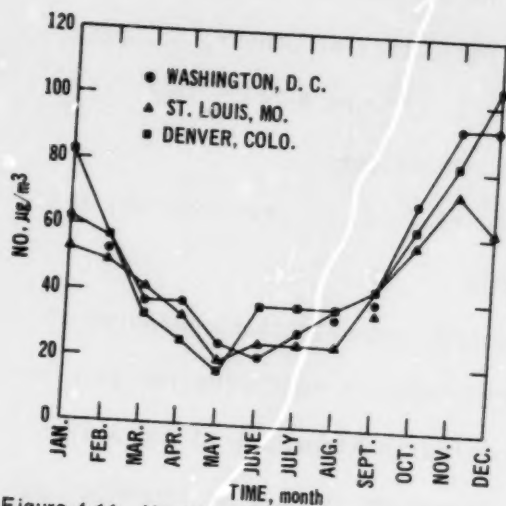


Figure 4-11. Monthly average of NO concentrations in three cities in the United States (data from 1969-1972)(13).

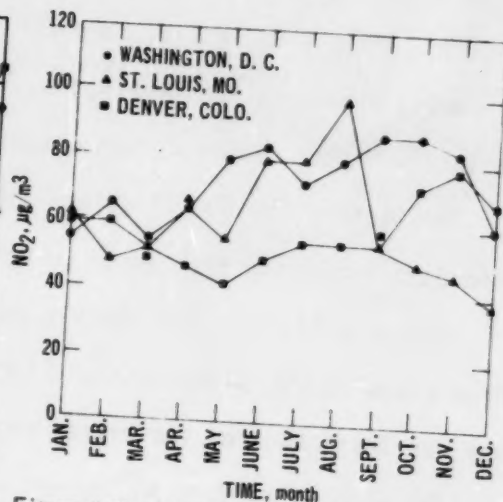


Figure 4-12. Monthly average of NO₂ concentrations in three cities in the United States (data from 1969-1972)(13).

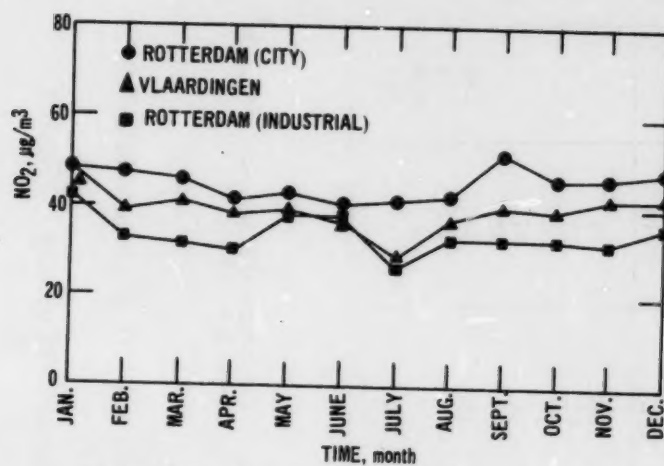


Figure 4-13. Monthly average of NO₂ concentrations at three sites in The Netherlands (14,15).

random variations are considered. A study by Brier (19) indicates that no adequate long-term data base is presently available for computing cyclical variations. Seasonal factors, on the other hand, are distinct and can be recorded. When data for several years are available, an average "seasonal index" can be calculated and applied to monthly means to obtain monthly values that are corrected for seasonal variations.

Table 4-1 presents the annual data for NO₂ concentrations at locations in Italy, The Netherlands, the United States, and West Germany.

5. Model for Relating Temporal Maxima

It is possible to convert the maximum concentration for one averaging time to that for another time. Larsen (21) has worked out formulas in which he computes the expected maximum concentration (C) for a selected averaging time by using the geometric mean concentration (M_g) for the area in question with its geometric standard deviation (σ_g), and the standard normal deviate (Z) for no more than one occurrence in $1.67 N$ trials.

His formula is:

$$C = M_g(\sigma_g)^Z$$

Table 4-1. ANNUAL AVERAGE CONCENTRATION OF NITROGEN DIOXIDE IN SELECTED EUROPEAN AND AMERICAN CITIES

Year	Concentrations, $\mu\text{g}/\text{m}^3$								
	Rome ^a	Rotterdam ^b city	Rotterdam ^b industrial	Vlaardingen ^b	Denver ^c	St. Louis ^c	Washington, C D.C.	Frankfort/ ^d Main	Munich ^e
1962							56	19	
1963							56	23	
1964							75	28	
1965							56	30	
1966								47	
1967		35			75	56		34	
1968		43	35		56	56		41	56
1969		43	40			38	75	100	132
1970		43	39	40		38			489
1971	30	45	34	38	56				827
	36			39	75	38	94		
							75		

^aConcentrations measured at ...

^aConcentrations measured at central city site (11).

^bConcentrations measured by Griess-Saltzman method. In 1970, the highest 3-hour concentration was 199 $\mu\text{g}/\text{m}^3$ measured in Vlaardingen on October 12 during the 1200 to 1500 hr sampling period (14,15).

^cConcentrations measured at CAMP stations by Griess-Saltzman method (13).

^dConcentrations measured at this site show an increasing trend between 1962 and 1970 which parallels that for CO. Griess-Saltzman method used for analysis (18).

^eConcentrations measured discontinuously at 25 sites near streets with high traffic density. A marked increase is shown in NO_2 level between 1967 and 1970 (20).

This formula and the associated mathematical model are based on the assumption that aerometric data are lognormally distributed. The model generally gives good estimates of expected maximum concentrations for averaging times of 1 hour to 1 day, even if aerometric data depart substantially from lognormal. The values of observed-hourly-average concentrations at the 0.1 to 30.0 percentile levels are used to calculate maximum concentrations for other averaging times. In addition, the model provides predictions of the 1-year concentration. The fit for averaging times from 1 day to about 6 months depends on how well actual aerometric data at a site fit the lognormal assumption. When the aerometric data fit lognormality well, then the model fits well for all averaging times from 1 hour to 1 year. Experience has shown that the model tends to overestimate expected concentrations for averaging times shorter than 1 hour. The equation given above is only valid if the data being used is lognormally distributed, which is not always the case with air pollution data.

C. EFFECTS OF METEOROLOGICAL FACTORS

At any given location, the NO_x concentration depends on many factors. Among them are the emission rate; the diffusion rate, which is meteorologically determined; and the reaction rate, which is both meteorologically (mixing depth as well as topographic influences) and chemically determined. All of these factors have an important effect on the distribution of pollution over a city. As with any primary pollutant, concentrations of NO (and therefore, subsequent concentrations of NO_2) on the upwind side of an area of sources are different from concentrations downwind. Spatial variations in concentration make the location of air-monitoring stations important, if representative air quality data are to be collected.

There is no reason to expect differences in meteorological influences on NO_x concentrations between Europe and the United States. Climatological influences, of course, are different between continents as they are between places within a continent.

As discussed earlier, the meteorology of an area also influences diurnal and seasonal variations; for example, daily minimum concentrations of NO_x usually occur during daylight hours at times of maximum ventilation and mixing. The amount of ultraviolet energy from the sun also governs the conversion rate of NO to NO_2 .

From a photochemical standpoint, the highest concentrations of NO_2 should occur during late spring and summer months. In most regions of the United States, radiation inversions during this period are often quite pronounced in the morning hours, but usually break by midday. On the other hand, during the fall and winter, when low sunlight intensity limits maximum photochemical processes, the atmosphere may remain stable for longer periods when the general circulation is weak. Such counteractive effects account for the relatively constant level of NO_2 throughout the year. An additional factor that moderates NO_2 levels is the incorporation of NO_2 into photochemical products. This incorporation has the effect of lowering daily average NO_2 values during periods of intense photochemical activity.

The effect of a stagnation period on the peak concentrations of NO and NO_2 is shown in Figures 4-14 and 4-15. The NO rise occurs when minimal dispersion of pollutants, because of stagnating meteorological conditions, coincides with maximum traffic conditions. The sharp midday drop in NO coincides with the NO_2 peak; the sharp NO_2 drop coincides with a total oxidant peak (Figure 4-16). The rapid afternoon rise in both

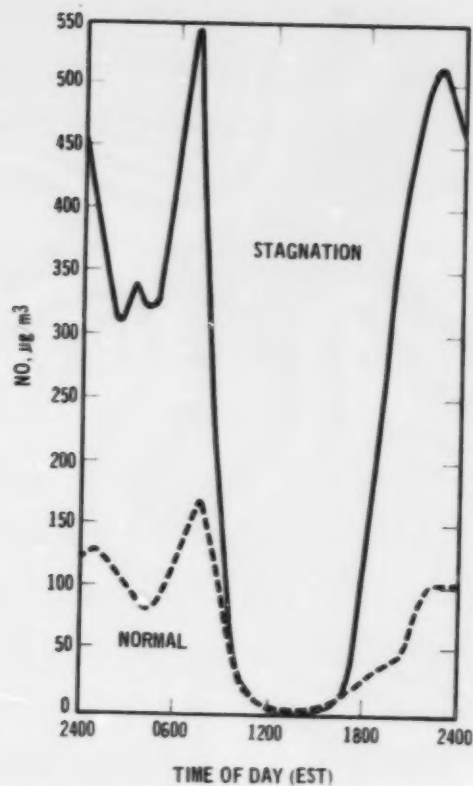


Figure 4-14. Diurnal variation of NO levels during 1963 stagnation in Washington, D.C., October 15 to 19, 1963 (15)

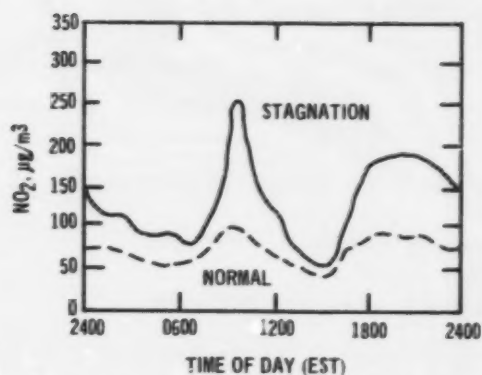


Figure 4-15. Diurnal variation of NO_2 levels during stagnation in Washington, D.C., October 15 through 19, 1963 (16)

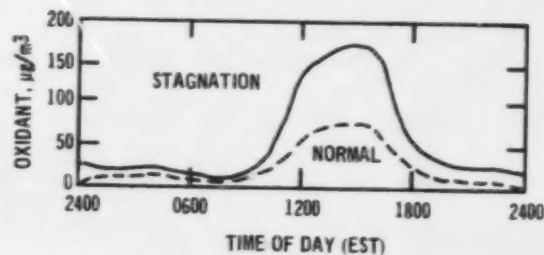


Figure 4-16. Diurnal variation of oxidant levels during stagnation in Washington, D.C., October 15 through 19, 1963 (16)

NO and NO₂ is, again, caused by stagnating conditions coupled with increases in vehicular traffic. In The Netherlands during the period of September 17 to October 7, 1971, an air pollution episode occurred in the densely populated areas of North and South Holland. Measurements made in Delft and Vlaardingen indicated the following maximum 30-minute concentrations of NO and NO₂ (µg/m³):

Delft	>450 NO;	131 NO ₂
Vlaardingen	472 NO;	340 NO ₂ .

Measurement of NO and NO₂ concentrations taken during 1969 and 1970 under similar conditions indicated a maximum of 1100 µg/m³ NO and 245 µg/m³ NO₂ for 30-minute means (15).

D. SUMMARY

Continuous measurement of the oxides of nitrogen by various monitoring networks has made it possible to compile selected time-averages of mean concentrations for selected time periods. From these values, various temporal patterns have been analyzed and related to photochemical and meteorological parameters.

Both NO and NO₂ concentrations display distinct diurnal variations dependent on the intensity of the solar ultraviolet energy and the amount of atmospheric mixing. These concentrations also vary with the traffic patterns in the sampling area.

Nitric oxide concentration shows a seasonal variation, with higher values occurring during the late fall and winter months. Nitrogen dioxide, however, does not display such distinct seasonal patterns.

The effect of meteorological factors on NO and NO₂ concentrations is well documented. Periods of stagnation in urban areas have resulted in high peak levels of NO_x and resultant high-oxidant levels.

Continuous measurement has indicated that peak values of NO are considerably higher than NO₂ concentrations.

One must also be extremely careful when evaluating and interpreting air quality data gathered from many sites. The air quality data obtained is greatly influenced by the location of the sampling stations, the conditions (meteorological as well as topographic) under which the samples were taken, the effects of the surrounding area, and many other factors.

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CHAPTER 5.

CHEMICAL INTERACTIONS OF NITROGEN OXIDES IN THE ATMOSPHERE

A. INTRODUCTION

This chapter examines the chemical relationship of nitrogen oxides (NO_x) to photochemical oxidants (OX) and to other products of atmospheric reactions, a relationship that encompasses several interrelated factors (1).

The most important aspect of this relationship with respect to air pollution is associated with the generation of oxidants. The generation of oxidants is a complex function of the interaction of certain hydrocarbons and hydrocarbon oxidation products with the nitrogen dioxide photolytic cycle (see Chapter 1). Nitrogen dioxide (NO_2), which initiates the process, is an efficient absorber of both the ultraviolet and visible portions of solar radiation (Figure 1-2). The ultraviolet portion of the radiation has sufficient energy to disrupt bonds in NO_2 and form two new species, nitric oxide (NO) and atomic oxygen (O). This atomic oxygen then reacts with air oxygen (O_2) to produce ozone (O_3), the principal oxidant in ambient air. The atomic oxygen and to a lesser extent the O_3 react with atmospheric hydrocarbons, especially the olefins and certain aromatics to form other pollutant products.

The NO formed in the initial NO_2 photolysis acts as a natural ozone regulator and forms oxygen and nitrogen dioxide in the reaction:



Because this reaction occurs almost instantaneously, appreciable concentrations of O_3 do not appear until NO has virtually disappeared from

the ambient atmosphere. Hydrocarbon interaction with the NO_2 photolytic cycle leads to the disappearance of NO with subsequent formation of NO_2 , and to the accumulation of hydrocarbon oxidation products and residual ozone (Figure 1-1).

The rates of formation and the steady-state concentrations of oxidants are a function of light intensity, the concentrations of hydrocarbons (HC) and NO_x , the HC to NO_x ratio, and the temperature. The rate of formation of oxidant is also influenced by the initial NO to NO_2 ratio, the relative humidity, and the occurrence of other air pollutant species. The nature of the HC molecule is an additional factor because individual hydrocarbons differ in their rate of interaction with the NO_2 photolytic cycle. Some hydrocarbons, such as methane and benzene, do not interact to form photochemical oxidants, at least not in synthetic systems. Others, certain olefins and substituted aromatics, for example, interact readily (2). The onset of the reactions is regulated by NO_2 concentrations. Minimal NO_2 concentrations delay, whereas higher NO_2 concentrations expedite the cycle.

This description of atmospheric reactions is greatly simplified and mentions only the major known reactions that account for the formation of photochemical oxidants. Although other reactions occur in the photochemical system, their roles are considered less important. Certainly, their involvement with NO_x is less clearly understood, and discussion of them is omitted in this document. They are covered, in part, in reference 1.

Subsequent, more detailed research may yet show that some of what are now considered minor reactions have essential roles in the regulation of atmospheric phenomena. These so-called minor reactions

may also become very important as the nature of ambient atmospheres changes in response to HC- and NO_x -control programs. This chapter does not discuss products of the photochemical reaction system, other than oxidants, in detail.

Photochemical oxidant relationships to eye irritants and to visibility-reducing aerosols suggest that the magnitude of effects varies directly with the oxidant formed, at least in the controlled, experimental system (1,2). Such an association, however, although typical of present photochemical smog systems, must be recognized as a generalization to which there are specific exceptions. Such exceptions sustain the need for continuous atmospheric studies in order to reassess the relationships between pollutant and effects, particularly as they may be affected by precursor-control strategies.

The major known variables that contribute to oxidant formation have been investigated extensively under controlled laboratory conditions (3-7). On the basis of such experimentation, it is possible to predict the effect of varied inputs on oxidant concentration and rates of formation. Extrapolation of laboratory results to ambient atmospheres, however, involves certain problems: 1. The mixing volume in laboratory simulations is a constant and favors a direct relationship between input concentrations of the precursors and the maximum concentration of result oxidant, which occurs several hours later. In contrast, the concentrations of both precursors and oxidants in ambient atmospheres are dominated by dispersion factors, which in turn alter the input/output relationship. 2. The definition of the variables is much more precise

in laboratory simulations than in routine atmospheric monitoring. In the laboratory, for example, the identity and concentration of each hydrocarbon in the system can be determined by gas chromatographic techniques. Routine atmospheric monitoring techniques have been largely restricted to measurements of total HC concentrations and, only recently, to measurements of total HC minus nonreactive methane. In addition, laboratory simulations have been largely carried out at concentrations higher than those observed in ambient atmospheres.

3. All laboratory simulations are, to some degree, affected by the experimental system. Thus, interaction of the gases with contamination on the walls of the testing chamber may affect the observed oxidant results.

In defining the OX-NO_x relationship, the approach was the same as the one used by Schuck et al. (8) to define the relationship of ambient HC concentrations to maximum daily oxidant values. The same patterns of chemical reactions and time-concentration relationships observed in the laboratory were assumed to apply in the atmospheric system and to affect oxidant levels in the same way. The approach, which can be termed an observational hypothesis, is based on several assumptions.

The basic assumption in the observational approach is that early morning HC and NO_x levels are indicators of the oxidant levels that will occur later in the day. Specifically, the 0600 to 0900 hr HC and NO_x levels are compared to the daily 1-hour maximum oxidant levels that normally occur between 1000 and 1400 hr. Because the time-con-

centration relationships are influenced by atmospheric dispersion factors, a specific ambient combination of HC and NO_x will not always result in a specific maximum oxidant value. The hypothesis provides rather for a wide range of maximum daily oxidant values to be associated with any given early-morning HC- NO_x combination. The precise oxidant concentration within that range will be regulated by the atmospheric stability factors for the day. For any concentration of precursors the hypothesis predicts maximum oxidant values near zero if substantial atmospheric instability follows the 0600 to 0900 hr period. Such instability causes the precursors as well as the products to disperse before they can interact and yield any appreciable amounts of oxidants. Conversely, the hypothesis allows for elevated oxidant values when the dispersion factors are more restrictive or when the atmosphere is stable following the 0600 to 0900 hr period. In those cases, precursors are trapped long enough for formation and accumulation of oxidants to occur. Between maximum and minimum atmospheric stability is a large range of dispersion factor combinations, which lead to intermediate maximum daily oxidant concentrations under the terms of the model.

Information from laboratory studies, however, suggests that the maximum attainable oxidant concentration will be limited by the available precursors regardless of how stable the atmosphere becomes. It is this upper-limit oxidant concentration that the observational approach attempts to define.

Many locations in Europe do not exhibit the same type of NO_x -HC-OX relationships that exist in the United States. In such places automobile traffic is not the main precursor of oxidant formation and

thus the empirical approach to oxidant formation used in the United States may not be totally applicable.

B. HYDROCARBON-NITROGEN OXIDES-OXIDANT RELATIONSHIPS

An initial attempt to explore the possible combined effects of HC-NO_x-OX is shown in Figure 5-1 for Pasadena, Calif. In this figure, upper-limit envelopes of HC levels as a function of oxidant and NO_x are superimposed on a graph showing the relationships of maximum oxidant levels to H₂O₂ concentrations.

The interdependent relationship among HC, NO_x, and OX concentrations in Figure 5-1 is in complete qualitative agreement with laboratory simulations (3-6). Available ambient data are too limited to clearly define these combinational effects. Furthermore, the HC values in Figure 5-1 represent calculated (2), rather than measured, nonmethane hydrocarbon concentrations. Data were taken at CAMP* stations on the days when nonmethane hydrocarbons were being measured. A base from these, involving 125 days of validated data, was used to construct the daily-maximum-oxidant isopleth lines as a function of the early-morning HC and NO_x values, which are shown in Figure 5-2. The dotted lines in Figure 5-2 are the levels of HC and NO_x associated with the reference 1-hour maximum oxidant concentration of 200 µg/m³ (0.1 ppm).

This similarity between laboratory results and the data from ambient atmospheres (Figure 5-1) lends validity to the measurements obtained with current air monitoring instruments. Furthermore, it suggests that the measured total hydrocarbon and the calculated

*Continuous Air Monitoring Projects of the United States Environmental Protection Agency.

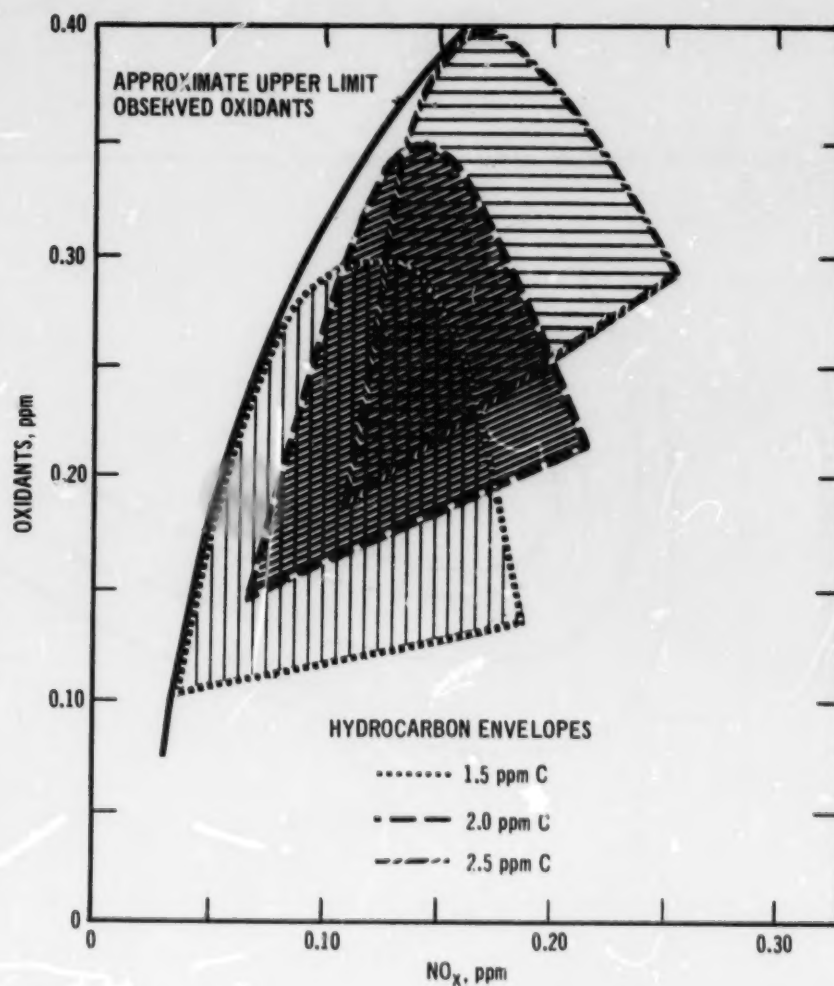


Figure 5-1. Hydrocarbon-oxidant envelopes superimposed on maximum daily 1-hour-average oxidant concentrations as a function of the 0600 to 0900 hr average of total nitrogen oxides in Pasadena, California, May through October 1967.

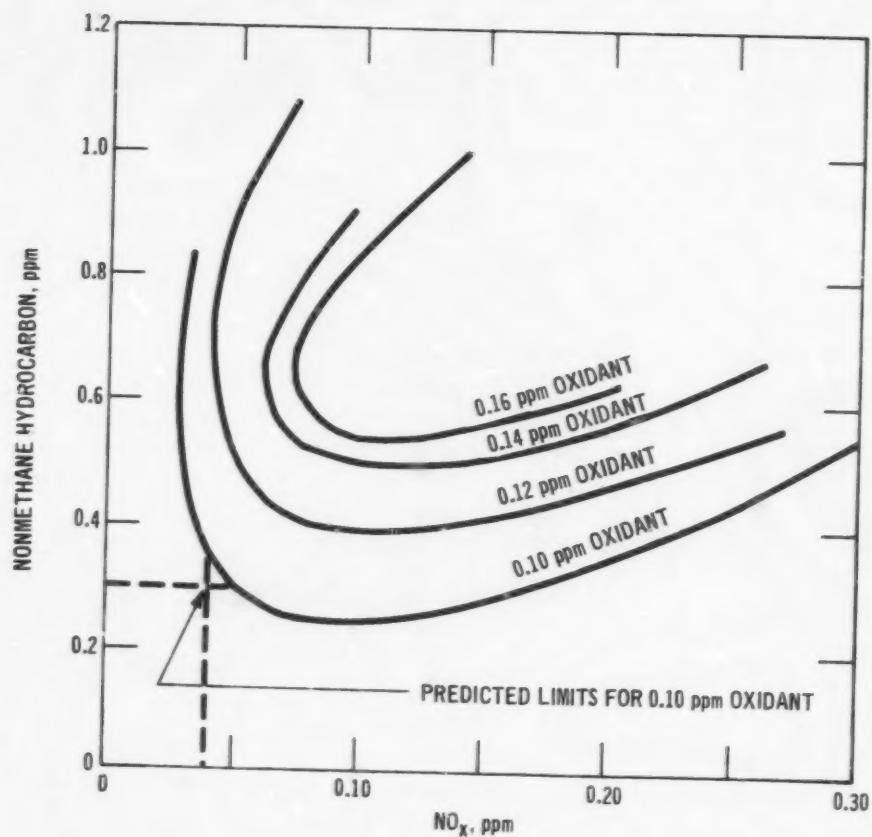


Figure 5-2. Approximate isopleths for selected upper-limit maximum daily 1-hour-average oxidant concentrations, as a function of the 0600 to 0900 hr averages of nonmethane hydrocarbons and total nitrogen oxides in Philadelphia, Pa., Washington, D.C., and Denver, Colo., June through August, 1966 through 1968.

nonmethane hydrocarbons are indeed proportional to the reactive HC fraction taking part in atmospheric oxidant formation.

In lieu of adequate atmospheric sampling data, laboratory simulations must be used as broad guidelines in discussing the interactions of the HC-NO_x system that produce ambient OX concentrations. At practically every HC-NO_x concentration, reduction in HC without NO_x reduction results in a reduction in O₃, whereas NO_x reduction without HC reduction does not always lead to a reduction in O₃.

Sources that emit different proportions of HC and NO_x likewise make different contributions to ambient levels of oxidants. Although the contributing factors are not yet identified, it appears that HC to NO_x ratios do vary in ambient atmospheres. Differing HC to NO_x ratios could arise from the range of operating conditions in automobile engines that result from variations in intake-air temperature and humidity.

C. LIMITATIONS AND INTERPRETATION OF OBSERVATIONAL APPROACH

The ideal approach to defining the HC-NO_x-OX interrelationships would take the form of a comprehensive model, which would take into account the interplay of emission rates, chemical reactions, and dispersion variables in space and time.

The absence of a fully validated model of this type required the development of the observational model discussed above.

In order to prevent misinterpretation of this observational approach, it is necessary to consider in detail the various factors involved.

1. Assumptions

One of the major assumptions is that the parameters affecting ambient oxidant concentrations are the same as the ones determined in laboratory systems. This does not mean that all known parameters have been delineated. In terms of certain major items, however, the laboratory results and ambient observations are qualitatively in agreement. In the atmosphere as in the laboratory, the major oxidant formed is ozone. Similarly, the conversion of NO to NO₂, the disappearance of certain reactive hydrocarbons, the appearance of aldehydes and peroxyacyl nitrates as intermediate products, and the dependence of the reactions on sunlight energy are apparent in both. In addition to the gross similarities, the rates of reaction and relative product yields are consistent.

Another major assumption is that early-morning precursor levels measured at a specific location are proportional to the maximum oxidant values that will be measured at this same location 2 to 4 hours later. This assumption implies both that meteorological conditions are homogeneous and that the precursor emissions are similar over large metropolitan areas. Although this assumption may be open to question, it is necessary at this time because the ambient-air monitoring data presently available are generally restricted to a single station in any one metropolitan area. The assumption has been justified by comparing data from several sites in Los Angeles County, which has one of the few comprehensive air-monitoring systems that have been in operation for many years. It was possible to show that oxidant concentrations measured simultaneously at several locations in a 2300 km² (900 mi²) area were similar and related (9).

Although evidence supporting the similarity of area-wide emissions is less substantial, the similarity of ambient concentrations of HC, NO_x , and OX for most days of the year over the entire Los Angeles basin suggests that the activities leading to emissions are reasonably consistent within a metropolitan area. The similarity of the data also tends to confirm the fact that meteorological conditions are generally homogeneous throughout the area.

On weekends during the summer season, however, a shift in observed emission patterns and resulting maximum oxidant concentrations could be related to the recreational activities of the populace (9). These alterations could only be demonstrated for stations separated by more than 32 km (20 mi), however. Otherwise, the assumption of the similarity between area-wide concentrations and subsequent maximum oxidant values appeared to be valid within a considerable distance of any one specific location.

The HC- NO_x -OX relationship in Figures 5-1 and 5-2 was obtained by comparing 0600 to 0900 hr precursor values to subsequent oxidant levels. The fact that such developed relationships show similar concentration and concentration-ratio effects in both field and laboratory observations strongly supports both of the major assumptions made in the observational approach. If the 0600 to 0900 hr precursor values were not a measure of subsequent maximum oxidant, it would be impossible to obtain atmospheric confirmation of complex chemical interactions such as shown in Figures 5-1 and 5-2.

2. Effects of Reductions in Photochemical Precursors

As noted earlier, reduction in NO_x without simultaneous reduction

in HC does not always lead to reduction in oxidants. Such laboratory findings indicate that if the objective is the control of oxidant then control of HC is the most appropriate step to take. The laboratory findings also raise the possibility that NO_x control by itself may, under certain circumstances, lead to increases in oxidant levels. Such increases, however, would only be characteristic of partial NO_x control because complete NO_x control, like complete HC control, would prevent formation of oxidant.

An additional consideration is the effect of HC or NO_x reductions on other products of the photochemical complex, such as eye irritants and visibility-limiting aerosols, which are also related to oxidant concentrations. Although these products vary with oxidant levels, the HC- NO_x mixture having the greatest potential for oxidant production will not necessarily correspond to maximum potential for eye irritants (5,10). The effect can be visualized in greatly simplified manner by examining known and expected reactions in a HC- NO_x system containing an excess of either HC or NO. Excess HC may act as a scavenger for oxidant and reduce oxidant levels with an accompanying increase in the eye irritant and other HC oxidation products. Excess NO acts as a scavenger for oxidant and thus reduces oxidant levels, increases NO_2 levels, and possibly decreases eye-irritant products. Unfortunately, much less is known about ambient levels and variations in eye irritants and aerosols than about the ambient levels of oxidants and NO_2 . For this reason, only generalized relationships of oxidant levels to eye irritation and visibility reduction can be defined. It is assumed that changes in all atmospheric pollutant concentrations in the years ahead will tend to modify these observed relationships. Such changes will most likely be

small, and though demonstrable in the laboratory, may not be observable in the atmosphere because all of the products are interdependent. Large reductions of HC, NO_x , or both, however, should reduce all of the pollutants and the resulting manifestations.

The information that is needed in the atmospheric data is a determination of the most logical precursor-reduction method that will guarantee reductions in O_3 and NO_2 concentrations to levels consistent with known public health requirements. The only approach that promises to accomplish this goal is a vigorous HC-reduction program coupled with NO_x reductions designed to reduce NO_2 levels below the health-related criteria level. The necessity for reducing NO_x below this suggested point cannot be ascertained at this time. If less stringent NO_x reductions (coupled with vigorous HC reductions) are sought, the possibility of causing a slight increase in oxidant values is minimized and, at the same time, the scavenging effect of NO for O_3 is maximized.

D. ADDITIONAL REACTIONS AND PRODUCTS OF NITROGEN OXIDES

In the previous sections, the major concern was the NO_2 photolytic cycle and its relationship to the major atmospheric oxidant, ozone. In addition to this major role nitrogen oxides also engage in reactions leading to formation of several nitrogen-containing compounds. Unfortunately, less is known about the fate of NO_x than is known about the fate of the hydrocarbons. In laboratory simulations, various investigators have been able to account for over 90 percent of the carbon atoms but only about 50 percent of the nitrogen.

One of the more important classes of nitrogen compounds resulting from atmospheric HC- NO_x interactions is known as the peroxy nitrates

(peroxyacetyl nitrates and peroxybenzoyl nitrates). Although these oxidants are minor from a concentration standpoint, peroxy nitrates are powerful eye irritants and phytotoxicants, and hence important contributors to photochemical air pollution. Peroxyacetyl nitrate (PAN), which has the highest atmospheric concentrations, has been extensively investigated. Pathways for formation of this class of compounds have been proposed, and several reaction systems have been used to produce these compounds in the laboratory; however, the specific mechanism involved in the atmosphere has not been established. Several other members of this class of peroxy nitrates that have been prepared and studied in the laboratory include peroxypropionyl nitrate, peroxybutyryl nitrate, peroxyisobutyryl nitrate, and peroxybenzoyl nitrate (11), but of these only peroxypropionyl nitrate has been found in ambient atmospheres (12); the formation of the initial member of the peroxy nitrate series, peroxyformyl nitrate, has not been accomplished in the laboratory or observed in ambient atmospheres. Recent investigations (13) suggest that peroxyacetyl nitrate and probably its homologues are important to the conversion of NO to NO₂ in ambient atmospheres.

Additional experimental evidence suggests that an undetermined fraction of the NO_x ends up as nitrous and nitric acid, and as trace amounts of nitrous oxide. Furthermore, nitrates have been identified as an important fraction of photochemically formed aerosols.

It is also important to recognize that there can be conversions in the atmosphere of NO₂ to particulate nitrate and other nitrate

species. Washout and/or deposition of these materials should not be ignored in terms of total effects upon the environment.

Bricard et al. (14) have observed that NO_2 in the atmosphere causes an increase in aerosol particulates and that, in the presence of $3760 \mu\text{g}/\text{m}^3$ (2 ppm) NO_2 , aerosols having a diameter of 10^{-6} to 10^{-7} cm are found to a maximum concentration of 150,000 particles per cubic centimeter. In addition they have observed that under the same irradiation conditions the photooxidation of SO_2 is increased when traces of NO_2 are present.

E. FUTURE RESEARCH

This examination of the role of NO_x in photochemical air pollution points out several areas requiring further investigation. The limitations of the observational hypothesis clearly indicate the need for:

- (1) a more comprehensive and definitive simulation model for NO_x , HC, and Ox,
- (2) more precise and definitive air-monitoring instruments, and
- (3) an intensified effort to identify the mechanisms of reactions and the fate of NO_x .

The observational model, for example, can only relate average concentration of precursors during an arbitrarily chosen time period (0600 to 0900 hr) to the upper-limit of maximum observed oxidant levels that occur later in the day. The model cannot, in its present form, relate rates of precursor emissions to rates of oxidant formation, nor does it define the relative contribution of various sources, either near or distant, to any given oxidant maximum.

Coupled with the need for broader instrumentation is the need for better air monitoring networks. In many cities the description of air quality and of changes in air quality still depend upon the data from a single station. A single station cannot adequately describe the variations in air quality that affect metropolitan areas occupying several hundred square miles. The air-monitoring stations and networks that do exist provide only a limited description of air quality. There is a dearth of monitoring information concerning specialized community exposures. For example, the air quality environment to which the populace is exposed while traveling on, or living adjacent to, heavily traveled roadways, cannot be adequately described.

Besides additional measurement of specific emissions and their products, the development of a more refined, detailed model requires more elaborate delineation of the meteorological parameters. At the present time, certain key factors, such as mixing height and sunlight intensity, are not measured on a routine basis in most polluted areas.

Better information is required to relate emission rates to air quality, as a function of source and time.

Although knowledge of the NO_2 photolytic mechanism and the ways in which this cycle interacts with reactive HC has a broad scope, the fate of up to 50 percent of the atmospheric NO_x is still not known. Details regarding these unidentified products are required in order to clearly assess their impact on health and welfare.

More precise and definitive instruments are now being manufactured for the measurement of HC. It appears to be important to not only measure

total HC but also to measure the separate HC species. This measurement is of prime importance in regions where the relative emission rates of the HC may change and where the automobile is not the principal source of the HC.

F. SUMMARY

The relationships between early-morning ambient HC levels and the maximum oxidant level observed later in the day have been examined through an atmospheric observational approach, which does not attempt to describe the complex relationships of Ox to ambient NO_x and HC levels. This document is concerned with a study of the complete HC- NO_x -Ox precursor - product relationship, and specifically with the changes in ambient oxidant and NO_x levels resulting from absolute and relative concentration variations of the HC- NO_x complex. The results of this examination are listed below.

1. The observational approach shows that the same reaction parameters that govern the HC- NO_x -Ox system in the laboratory operate in ambient atmospheres.
2. The ambient levels of 0600 to 0900 hr precursors, HC and NO_x , are a reliable indicator of the maximum attainable 1-hour-average-oxidant concentration that occurs 2 to 4 hours later, between 1000 and 1400 hr.
3. The atmospheric conditions that lead to maximum oxidant potential, i.e., low wind-speeds, high temperature, intense sunlight, and surface inversions, occur in many parts of the world.
4. Independent studies of the effect of variations in either HC or NO_x level are not possible in ambient atmospheres. Atmospheric observation shows, however, that when the calculated 0600 to 0900 hr

nonmethane hydrocarbons are in the approximate range of 200 to 930 $\mu\text{g}/\text{m}^3$ (0.3 to 1.4 ppm C) and the 0600 to 0900 hr NO_x value is approximately 80 $\mu\text{g}/\text{m}^3$ (0.04 ppm), the maximum daily oxidant will reach 200 $\mu\text{g}/\text{m}^3$ (0.10 ppm) on only 1 percent of the days.

Further observation of the data base shows that 80 $\mu\text{g}/\text{m}^3$ (0.04 ppm) NO_x occurs simultaneously with calculated nonmethane HC concentrations ranging from 200 to 930 $\mu\text{g}/\text{m}^3$ (0.3 to 1.4 ppm C). Similarly, observation of the 200 $\mu\text{g}/\text{m}^3$ (0.3 ppm C) nonmethane HC level shows NO_x in the range of 80 to 320 $\mu\text{g}/\text{m}^3$ (0.04 to 0.16 ppm).

5. Laboratory studies do permit the independent evaluation of the effects of varying either HC or NO_x . Using such studies as guidelines, control agencies can consider a combinational HC and NO_x reduction program applicable to polluted ambient atmospheres. The data base suggests that reductions in HC should be the primary step for control of oxidants. Coupled with HC control, NO_x must be controlled at a level that will hold ambient NO_2 values below the level of adverse health effects.

6. Nitrogen oxides have also been implicated in the formation of peroxy nitrates and aerosols. The precise mechanism of formation has yet to be elucidated, but, to the extent that oxidant levels are a measure of the intensity of the effects of the photochemical complex, the control of NO_x and HC to the suggested levels can be expected to control all undesirable aspects of NO_x and its products.

7. Conditions that exist in the United States do not always apply in Europe, particularly in those areas where the automobile is not the principle source of NO_x and HC.

These results are largely based on examination of current ambient atmospheric data as defined by current monitoring techniques. It

can be expected that these techniques will be modified to provide improved information. Furthermore, the application of emission-control measures can be expected to change the relative, as well as the absolute, concentrations of atmospheric contaminants. All of these factors dictate the need for a continual reexamination and updating of the observations in this chapter.

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CHAPTER 6

EFFECTS OF NITROGEN OXIDES ON MATERIALS

A. INTRODUCTION

Field study and laboratory research has successfully shown that atmospheric levels of nitrogen oxides (NO_x) can produce detrimental effects on textile dyes and additives, natural and synthetic fibers, and metals. Although not as well known as those caused by sulfur dioxide or ozone, these effects, nevertheless, are important and represent a significant economic burden; annual damage is estimated at three-quarters of a billion dollars in the United States (1).

Nitric oxide (NO) and its principal reaction product, nitrogen dioxide (NO_2), participate in a number of complex atmospheric reactions. Eventually, atmospheric processes bring the NO_x to the nitric acid stage where it rapidly reacts to produce various particulate nitrates. This chapter discusses only the material effects that are attributed to NO_x and particulate nitrates, but this limitation does not preclude the possibility that other reactants such as nitric acid (HNO_3) can cause damage. One must not, however, lose sight of the role of NO_x in the photochemical formation and buildup of ozone and other oxidants, as well as in the photooxidation of sulfur dioxide in the presence of reactive hydrocarbons to produce sulfuric acid aerosols. The photochemical reaction products are believed to cause more direct damage than NO_x ; thus, control and reduction of NO_x should

also be valuable in reducing damage from these products. The document, Air Quality Criteria for Photochemical Oxidants (2), discusses in detail the effects of photochemical pollutants on materials.

B. EFFECTS ON TEXTILE DYES

1. Acetate Rayon Fading

a. Historical Background

Early in this century, a German dye manufacturer investigated some unusual cases of dye fading on stored woolen goods (3). Fading was most noticeable on the edges of the goods, and the primary cause was traced to NO_x in the air. Open electric-arc lamps and incandescent gas mantles were major sources of these pollutants by means of high-temperature fixation of atmospheric nitrogen. The investigators found that all the susceptible dyes contained free or substituted amino groups, and they suggested that these might become either diazotized or nitrosated by the NO_x .

In subsequent years, the increased replacement of older forms of lighting with electric filament lamps led to a general decline in the wool-fading problem. In the mid-1920's, researchers developed and introduced a new fiber, cellulose acetate rayon. Traditional dyes were of little use on this fiber, but chemists soon developed an entirely new line of dyestuff called disperse dyes. Many of these dyes are derived from anthraquinone and therefore contain amino-groups, the same groups the German investigators had previously found susceptible to NO_x fading.

Shortly thereafter a puzzling type of fading began to occur increasingly on dyed acetate. Blue, green, and violet shades of fabrics, either stored or in use, faded mysteriously. Because this fading was frequently observed in rooms heated by gas heaters, it was called "gas-fume fading" or "gas fading."

During the 1930's, acetate fading became a serious problem. Dye and fiber chemists, apparently unaware of the earlier German work, devoted considerable efforts toward a solution. These efforts culminated in 1937 when Rowe and Chamberlain (4) systematically investigated the fundamental chemistry of dye degradation and independently reached the same conclusions as the earlier German team. Since then, much research has been carried out in an effort to understand gas fading and to develop ways of preventing it (5-7).

b. Gas-Fading Characteristics

Gas fading of vulnerable dyes on acetate is marked by a definite and characteristic reddening of the fabric. This reddening effect took on special importance in the mid-1950's when investigators discovered that ozone also fades many of the same dyes found to be sensitive to NO_x . In many cases the characteristic reddening enables scientists to discriminate between gas fading and the bleached, washed-out fading that ozone produces.

Despite earlier research reporting that pure NO slightly fades some disperse dyes (6), current opinion (3,8) favors NO_2 as the fading agent. Recent controlled environment studies support this opinion (9). Furthermore, acetate fibers are excellent absorbers of NO_2 (8), and

this property undoubtedly also plays an important role in dye-fading mechanisms.

The disperse dyes sensitive to gas fading have an amino anthraquinone structure. The reactions that cause fading include nitrosation, diazotization, and oxidation (3). Blue dyes are especially susceptible; some violets and reds also fade. Even blends of susceptible dyes with resistant dyes are subject to gas fading.

c. Test for Sensitivity

Recognizing the importance of fading caused by NO_x , the American Association of Textile Chemists and Colorists (AATCC) developed a fading-test procedure that they tentatively adopted in 1941 and formally approved in 1957. It is presently designated as Standard Test Method 23-1972, Colorfastness to Burnt Gas Fumes (10). This method calls for suspending test specimens along with a control sample in a chamber, and exposing them to combustion gases from a gas burner that has been adjusted so that the chamber temperature does not exceed 60 °C. Based on measurements using the Griess-Saltzman method and 10-minute sampling intervals, the resulting concentration of NO_2 is about 2.5 mg/m³ (1.5 ppm). Specimens remain in the chamber until the control sample shows a change in shade corresponding to a fading standard. When this happens, the specimens are said to have had a treatment equivalent to 6 months of actual exposure to average air, as represented by three separate locations in southern New Jersey. If the test specimens do not fade appreciably after one exposure period, the procedure is repeated (using a fresh control sample) as many times as necessary to make an evaluation. Dyed fabrics are

classified and rated according to the number of exposures necessary to produce appreciable changes in shade.

d. Attempts at Protection

To alleviate the fading problem, researchers have developed a number of chemical inhibitors that can be added to dyed fabrics to provide a selective reaction with NO_x (8,11). Inhibitors, unfortunately, are only temporarily effective; they are eventually used up and the dye again becomes vulnerable to fading. Subsequently, researchers developed dyes that were resistant to fading, but those dyes had poor lightfastness. In the 1950's, chemists synthesized new dyes that resisted the fading effects of both NO_x and light (8,12,13). These dyes, however, are more expensive and have poor dyeing properties that result in slower processing rates and require greater care during application. Other means of circumventing the fading problem include the use of alternative fibers or fibers with colored pigments incorporated in them.

e. Present Status

Because these vulnerable disperse dyes on acetate are moderately priced and possess desirable dyeing properties, they are still specified for some products regardless of their NO_x fading shortcomings. As a result, costly gas-fading incidents still persist despite the use of protective inhibitors (14-16). Fading of acetate linings in men's suits has been a particularly vexing problem. The most costly incidents have taken place during the storage of fabrics and end-products in warehouses; entire truckloads of materials have

either been sold at prices below cost or returned to the producers.

2. Cotton and Viscose Rayon Fading (Cellulosics)

Although NO_x fading of certain disperse dyes on cellulose acetate fabrics is now well documented, the textile industry has paid little attention to the fading caused by pollutants on cotton and viscose rayon (collectively referred to as cellulosics). Consumers and retailers have registered color-change complaints, but textile producers generally attribute this fading to light rather than pollutant effects.

An early indication of the cotton problem occurred in the mid-1950's. Dye chemists investigated a series of complaints that some colored cotton fabrics were fading during the drying cycle in home gas-fired dryers (17). The investigators traced the fading to oxides of nitrogen formed during the combustion of natural gas used to heat the dryers. Fading occurred only while the textile materials were moist. A research program conducted about 10 years later confirmed the gas-dryer fading problem and found that NO_x levels (expressed as NO_2) in such dryers ranged from 1.1 to 3.7 mg/m^3 (0.6 to 2 ppm) (18). NO_x levels were measured using a modified Griess method.

Within the last decade, additional evidence of this type of fading has emerged. When exposed to a number of different field environments in the absence of light, some dyed cellulosic fabrics showed fading after 2 to 3 months (19,20). Fading occurred in certain blue and green shades, representing dyes from four major classes: direct, sulfur, vat, and reactive. Laboratory exposure of these shades to the standard gas-fading test procedure did not produce fading (21).

This test procedure was designed to evaluate dyed acetate fabrics and had no provisions for controlling relative humidity because humidity is not a critical factor in acetate fading. The field exposures, however, indicated that relative humidity might be an important controlling factor in cellulosics fading. Subsequent laboratory exposures to the gas-fading test procedure were therefore conducted under high-humidity conditions (probably greater than 50 percent). The results were dramatic; the same concentrations of NO_x produced color changes that generally agreed with the field results. Presently, the textile-dye industry is considering modifying the gas-fading test procedure to require humidity-controlled conditions (21-23).

3. Yellowing of Whites

A new problem that has received little publicity, but is of considerable concern to the textile industry, is the yellow discoloration of undyed-white or pastel-colored fabrics (18,23). These fabrics may be woven from any number of common fibers, but most of the discoloration has occurred on nylon, acetate, and permanent-press materials. Discoloration has usually occurred on items stored or on display, including dresses, shirts, curtains, and lingerie. Returned items have represented major losses to some textile companies.

Because most discoloration occurs on whites, dyes were ruled out as a source of the problem. Investigators turned to various additives that are applied to fibers and fabrics to enhance certain properties. These include optical brighteners; cationic antistatic, and soil-release finishers; softeners; and resinous processing agents.

When tested by standard laboratory procedures, including the gas-fading procedure, many of these additives yellowed on exposure to NO_x . Washing the fabrics sometimes removed the yellow discoloration, but this is impractical for items that yellow in warehouses or on display. Today, the problem is best solved by selecting resistant additives. This may result in diseconomies, but the textile industry and retailers recognize that some action must be taken to avoid an increasing number of complaints about the discoloration of whites.

4. Recent Field and Laboratory Exposures

a. Field Study

The AATCC and the United States Environmental Protection Agency (EPA) conducted a comprehensive field study to assess color changes of dyed fabrics exposed to different kinds of polluted environments (24). A total of 67 dye-fabric combinations were selected for testing. The fibers from which the fabrics were woven included the cellulose, acetate, wool, nylon, polyester, and acrylic. The dyes consisted mainly of those commonly used on these fibers and represented various degrees of known susceptibility to air pollution fading. Fabric samples were exposed in light-tight cabinets similar to those used in previous AATCC service trials. Individual cabinets were set up at exposure sites in Los Angeles, California; Tacoma, Washington; Chicago, Illinois; Washington, D. C. and at corresponding rural control sites for each of these cities. In addition, single sites were located in Cincinnati, Ohio; Phoenix, Arizona; and Sarasota, Florida. These 11 sites represented a cross section of various types of pollution and climates. Sulfur dioxide, nitric oxide, nitrogen dioxide, oxidant, and hydrocarbon concentrations

were continuously measured near the urban sites in Chicago, Cincinnati, Los Angeles, and Washington. The study was carried out over a 2-year period and consisted of 8 consecutive 3-month seasonal exposures commencing with the spring season (March-April-May, 1966). Using a precision photoelectric colorimeter to measure color before and after exposure, color changes were calculated for all dyed fabric samples at all sites for all seasonal exposures.

Color change data along with air pollution and weather measurements were statistically analyzed in an effort to identify factors causing fading. Of the 67 fabrics exposed, 24 either did not fade or faded only insignificantly and therefore were eliminated from statistical consideration; the remaining 43 fabrics faded in appreciable amounts. Most of these fabrics faded significantly more at urban sites than at corresponding rural sites, and the amount of fading varied among metropolitan areas and among seasons. Air pollution was assumed to account for most of the environmental differences between urban and rural sites.

Further analysis showed that of the pollutants measured, sulfur dioxide, nitrogen dioxide, and oxidants (mainly ozone) appeared to be those most responsible for causing fabrics to fade. Temperature and humidity seem to have little influence on fading when dyed fabrics are exposed in essentially pollution-free environments. In polluted environments, however, high temperature and humidity may accelerate fading. An analysis of the results showed that nitrogen dioxide was a significant pollutant factor (but not necessarily the only pollutant factor) for seven of the 43 fabrics. In many cases, however, it was impossible to specifically attribute the effects to nitrogen dioxide as these effects are confounded with the effects of other pollutants.

b. Laboratory Studies

The United States Environmental Protection Agency also conducted laboratory studies that were designed to directly assess the effects of individual pollutants on dyed fabrics (9). Investigators exposed 20 dye-fabric combinations for 12 consecutive weeks in the absence of light to individual controlled environments consisting of clean air (control) and clean air contaminated with single pollutants. The pollutants were sulfur dioxide, nitric oxide, nitrogen dioxide, and ozone. Controlled exposure conditions consisted of two pollution levels, in addition to clean air, under four combinations of temperature and relative humidity: 32 °C, 50 percent RH; 32 °C, 90 percent RH; 13 °C, 50 percent RH; and 13 °C, 90 percent RH. Nitric oxide (NO) concentrations were 120 $\mu\text{g}/\text{m}^3$ (0.1 ppm) and 1200 $\mu\text{g}/\text{m}^3$ (1.0 ppm); nitrogen dioxide (NO₂) concentrations were 90 $\mu\text{g}/\text{m}^3$ (0.05 ppm) and 940 $\mu\text{g}/\text{m}^3$ (0.5 ppm). All pollutants were continuously monitored; a modified Griess-Saltzman method was used to analyze nitrogen oxides. The 20 fabrics selected were a cross section of those that showed the greatest tendency to fade during the field study previously described (24), together with several non-faders that served as controls.

The investigators found that nitric oxide (NO) was an insignificant factor in causing these fabrics to fade; this agrees with the findings of previous research. On the other hand, NO₂ was the most potent pollutant evaluated, causing the greatest amount of fading on 13 of the fabrics. Fading occurred on cotton, rayon, acetate, and nylon fabrics. Furthermore, the rates of fading generally decreased with time.

Although the high-exposure levels of NO₂ produced the most pronounced fading effects, low levels, nevertheless, caused readily visible color

changes in a number of the fabrics. Relative humidity and to a lesser extent temperature were significant factors in accelerating fading. The exposure results also showed that fading in most cases is dependent on the nature of the fiber substrate. Acetate fabrics dyed with disperse blue No. 3 faded two to five times more severely than nylon fabrics did with the same dye. Likewise, disperse blue 27 on acetate faded severely, but the same dye on polyester did not fade.

C. EFFECTS ON TEXTILE FIBERS

1. Cellulosic Fibers

Researchers have not studied the direct effects of NO_x on cellulosic fibers, but Morris et al. (25) conducted a field study in Berkeley, California, in which they attributed observed damage to ambient levels of NO_x . They exposed combed cotton yarn samples at a 45-degree angle in cabinets facing south. Polyvinyl fluoride film, rather than glass, was used to cover the cabinets in order to allow a greater amount of sunlight to enter. One cabinet served as a control, in which entering air was filtered through carbon canisters. Ambient air was circulated through the other cabinet. (The investigators did not note the rate of air change.) Some samples in each cabinet were exposed directly to daylight, and others were shaded. Samples were exposed for three separate 28-day periods (December through February), as well as for consecutive combinations of these three periods (Table 6-1). During exposure, air pollution and weather measurements were made as shown in Table 6-2.

At least 20 yarn specimens were evaluated for each exposure period. The investigators assessed deterioration by measuring loss in breaking strength. Table 6-1 shows mean values for the percent loss in breaking

Table 6-1. BREAKING-STRENGTH OF COTTON YARN SAMPLES EXPOSED TO AIR AND SUNLIGHT IN BERKELEY, CALIFORNIA

Exposure		Breaking strength, % loss	
Number of days	Period ^a	Filtered air	Unfiltered air
28	I	11	15
28	II	15	18
28	III	15	16
56	I, II	20	24
56	II, III	19	29
84	I, II, III	26	32

^aI-December, II-January, III-February.

Table 6-2. AIR POLLUTANT LEVELS^a AND WEATHER MEASUREMENTS

Exposure period	Total oxidant,		Nitric oxide,		Nitrogen dioxide,		Temp, °C	Total sunshine % days	Rain in.
	ppm	µg/m ³	ppm	µg/m ³	ppm	µg/m ³			
I	0.03	60	0.19	230	0.08	150	10	100	0.5
II	0.03	60	0.23	280	0.08	150	10	100	6
III	0.03	60	0.07	90	0.05	90	10	72	10

^aFor clock hour with highest average value.

strength for unshaded samples, exposed to filtered and unfiltered ambient air, for the various exposure periods. An analysis of variance of these mean loss values revealed that unfiltered air deteriorated the cotton yarn to a significantly greater extent than filtered air. The shaded samples did not develop a corresponding difference between filtered and unfiltered air. Although textile investigators are well aware of the pronounced deteriorating action of direct sunlight, the results of this study serve to emphasize the importance of sunlight in stimulating reactions between some air pollutants and materials. It is noteworthy that the smallest difference between breaking-strength losses for filtered and unfiltered air occurred during Period III (February). This period had the most rain, which cleans the air; the lowest levels of NO_x ; and the lowest total hours of sunshine. Although it was impossible to designate the aggressive pollutant in this study, the investigators proposed that nitrogen oxides, either directly or indirectly, were instrumental in causing damage. Sulfur dioxide was not measured during the study, but was known to be low from previous measurements.

The investigators did not mention the fact that, although the filter material, activated carbon, absorbs NO_x effectively, it absorbs NO poorly. Levels of NO in the filtered air cabinet could, conceivably, have contributed to the decrease in breaking strength. If this were the case, cotton specimens exposed to clean air would show a smaller loss in breaking strength, and the relative pollution effect would increase.

2. Synthetic Fibers

Several investigators working with synthetic fibers have found that nitrogen oxides under laboratory conditions, are capable of

causing damage. They reason, therefore, that these pollutants are potential threats under ambient conditions. Damage reports from the field, however, have been few and only one incident has been documented.

In March 1964, an episode of runs in nylon stockings worn by women occurred in the vicinity of a demolition project in downtown New York City (26). Investigators identified the agent causing the damage as nitrogen dioxide gas released during dynamite blasting operations. Local weather conditions at that time were unfavorable in that a temperature inversion existed along with wind stagnation and high humidity. The investigators proposed that the combination of these conditions in the presence of abnormally high levels of released NO_2 and dust produced nitric acid aerosols that damaged the nylon stockings.

Travnicek (27) gathered information on incidents involving air pollution damage to nylon stockings and, noting the New York City episode, offered the opinion that "The corrosive effect of nitrogen oxides is rather high not only for nylons but for practically all other fiber forming polymers because it combines acid corrosion and oxidation."

Because nitrogen oxides are major components of auto exhaust, the laboratory research that Travnicek (27) carried out may be significant. He exposed samples of synthetic fibers (only nylon is identified) for 50 hours to a continuous flow of undiluted auto exhaust in a controlled environment chamber illuminated by artificial sunlight. Under these exposure conditions, Travnicek found that the physical properties of the fibers changed, and that the changes reflected the

interplay of two reactions: cross-linking reactions, probably the result of aldehydes, and depolymerization reactions largely caused by light. Furthermore, he observed that, to a certain degree, some light stabilizers and dyes, because of preferential reactions with oxidizing agents, protected the fibers from degradation. Protection is most evident when nitrogen oxides and sunlight transform components of exhaust gases into oxidizing agents. When fibers were exposed to dilute exhaust gases, which simulated summer-time conditions on traffic-congested streets, Travnicek found that the diluted gases became a potential menace to these fibers only if given sufficient time and light to produce oxidizing substances. He did not define "sufficient time and light."

According to Travnicek, oxides of nitrogen may attack and damage fibers by virtue of the formation of nitric acid droplets, by direct oxidation, and by conversion of other exhaust components into harmful oxidizing agents.

The oxides of nitrogen may pose a problem for Spandex, a synthetic elastomeric fiber. On exposure to the standard gas-fading test procedure, Spandex develops a yellowish discoloration (23). This is not a case of dye fading because the exposed material contained no dyes or color pigments; rather the nitrogen oxides react directly with the polymer. Although the laboratory test exposure levels are somewhat higher than measured levels in ambient air, a potential problem may develop under ambient conditions. So far, however, few complaints from the field have been registered.

Citing recent technology on the dyeing of DuPont nylon yarns, Trommer (28) states that nylon polymers are subject to oxidation by nitrogen oxides and other oxidants, and may themselves serve as reducing agents. If oxidation occurs, nylon fibers would have less

affinity for acid dyes. Natural (undyed) continuous filament styling yarns, which have a high capacity for acid dyes, are especially sensitive to oxidation reactions. Trommer cautions that these nylon yarns should not be exposed for prolonged periods to factory environments in which fork-lift trucks emit exhaust fumes.

In laboratory research that Zeronian et al. (29) recently completed, fabric samples of modacrylic (Dynel), acrylic (Orlon), nylon 66 and polyester (Dacron) were simultaneously exposed to artificial light (Xenon arc) and clean air contaminated with $349 \mu\text{g}/\text{m}^3$ (0.2 ppm) NO_2 at 48°C and 39 percent relative humidity. Nitrogen dioxide was continuously analyzed using the Schulze modification of the Griess-Saltzman method. During exposure, the fabric samples were sprayed with water continuously for 18 minutes every 2 hours. Damage by NO_2 was measured by comparison with fabrics exposed to the same environmental conditions but without NO_2 . After exposure to these controlled conditions for 7 days, Zeronian found that NO_2 did not affect the modacrylic fabrics, but appeared to slightly affect the other fabrics. The evidence for nylon appeared to be the strongest, although the investigators emphasize that the results for all fabrics were not clear and more research was needed.

D. EFFECTS ON NICKEL-BRASS ALLOYS

1. Stress-Corrosion

In 1959 the Pacific Telephone and Telegraph Company noticed considerable breakage of their nickel-brass (65Cu-23Zn-12Ni) wire springs in some relays located in Los Angeles area offices (30-32).

Failures often occurred within 2 years after installation. These failures were totally unexpected since the wire springs had been used with excellent results for years throughout the nation. Investigators found that breakage occurred on wires that were under moderate stress and a positive electrical potential, and it was concluded that the failure mechanism was a form of stress-corrosion-cracking. Bell Laboratories subsequently showed that high-nitrate concentrations in airborne dust, which had accumulated on surfaces adjacent to cracked areas, produced the failures. The nitrate content of dust from Los Angeles is from 5 to 15 times greater than from most eastern and midwestern cities. Furthermore, Los Angeles dust consists of light-colored, very fine, claylike materials and considerable organic matter in a highly oxidized, polar condition. This combination results in dust that is more sensitive and reactive to moisture than the carbonaceous, oily, siliceous, high-sulfate content of most eastern dusts. Nitrates are also more hygroscopic than sulfate salts. Additional tests have shown that failures take place only when surface nitrate concentrations are above $2.4 \mu\text{g}/\text{m}^3$ and when the relative humidity, a very important controlling factor, is above 50 percent. Other salts will cause stress corrosion, but only when the relative humidity is greater than 75 percent; for sulfate salts it must exceed 95 percent.

Sometime after this stress-corrosion problem was first observed in Los Angeles, scattered failures were reported, not only in wire springs, but in other nickel-brass components elsewhere in California, and in New York City and Philadelphia. Westinghouse (31) has reported failures in Texas and New Jersey.

Bell Laboratories (32) also reported a totally different type of corrosion problem that has been observed in such widely scattered locations as Cincinnati, Cleveland, Detroit, Los Angeles, New York and Philadelphia. The nickel bases of palladium-capped contacts of crossbar switches corroded forming bright greenish corrosion products that gradually crept up over the palladium cap of the contacts, resulting in electrically open circuits. Investigators concluded that the "creeping green" corrosion was promoted by the presence of anions, principally nitrates, in accumulated dust. Nitrates in urban atmospheres have been identified as one of the end products of the photochemical reactions between oxides of nitrogen and hydrocarbons. In Cincinnati and Philadelphia, the cities for which data are available, the 1965 average airborne nitrate particulate concentrations were 3.4 and 3.0 $\mu\text{g}/\text{m}^3$ respectively. The corresponding average gaseous NO_x levels were 124 and 158 $\mu\text{g}/\text{m}^3$ (0.066 and 0.084 ppm).

2. Protection

The telephone company took several measures to correct the stress-corrosion problem. Researchers found that when zinc is left out of the nickel-brass alloy, stress corrosion no longer occurs. To prevent future problems, a copper nickel material was specified for subsequently manufactured wire-spring relays. In high-nitrate areas, local central offices protected existing nickel-brass relays by installing high-efficiency filters in outside-air intakes of ventilating systems, and by redesigning their cooling systems to keep relative humidity below 50 percent.

E. MISCELLANEOUS MATERIALS

Jellinek (33) presents evidence that NO_2 at concentrations of 1.88 to 9.40 mg/m^3 (1 to 5 ppm) causes chain scission and cross-linking in some polymeric materials. Nylon and certain elastomers--butyl, polybutadiene, and polyisoprene--are quite sensitive; polyethylene and polypropylene are less sensitive. Vinyl, styrene, acrylic, vinylfluoride, acrylonitrile, and carbonate polymers appear to be resistant.

F. FUTURE RESEARCH

Although qualitative knowledge of the detrimental effects of NO_x on various materials is documented and recognized, reliable dose-response data is needed as is improved economic estimates of materials damage. More information is needed on the effect of NO_x on building materials and works of art and the effect of the interaction of pollutants including NO_x , nitric acid, and particulate nitrates on materials.

G. SUMMARY

Investigators have found that oxides of nitrogen and their corresponding reaction products cause certain textile dyes to fade, cause some textile additives to yellow, deteriorate cotton fabrics, and accelerate corrosion of certain metals. The most serious effects concern textile dyes and additives. In the United States annual damage to materials by atmospheric NO_x is grossly estimated at three-quarters of a billion dollars.

Many years ago, complaints by retailers prompted the discovery that NO_x fades a number of sensitive, disperse dyes used on cellulose acetate fibers. The sensitive colors were mainly shades of blue. To correct this fading problem, dye chemists have developed

inhibitors, which provide temporary protection, and fade-resistant dyes. In both cases and especially in the latter, the end result is a more expensive fabric.

During the last decade or so, investigators found that certain blue and green shades of dyed cellulose faded under high-humidity conditions. They first encountered this problem when investigating complaints that cotton fabrics faded during the drying cycle in home gas-fired dryers. They found that oxides of nitrogen, which are among the products of combustion of natural gas, readily reacted with some dyes under moist conditions. NO_2 levels in the dryers ranged from 1.1 to 3.7 mg/m^3 (0.6 to 2 ppm). Later, field exposures, in the absence of light, showed fading occurred in certain dyed cellulosic fabrics. Previous laboratory exposures to NO_x had not faded these fabrics. Subsequent laboratory exposure to NO_x , under conditions of high humidity, did produce fading in these fabrics and confirmed the importance of atmospheric moisture in the fading reactions.

A new problem facing the textile industry concerns the yellow discoloration of undyed-white and pastel-colored fabrics. Chemists have traced this yellowing to the action of NO_x on certain additives applied to fabrics to enhance their marketing properties. These additives include optical brighteners, softeners, antistatic and soil-release finishes, and resinous processing agents. To prevent this yellow discoloration, textile processors must be critical in selecting NO_x -resistant additives, which are generally more costly.

Recent controlled environment chamber exposures revealed that 13 out of 20 dye-fabric combinations developed visible color changes when exposed for up to 90 days to $90 \mu\text{g}/\text{m}^3$ (0.05 ppm) NO_2 .

Information concerning the damaging effects of NO_x on textile fibers is meager. One study attributed modestly increased losses in fiber strength of cotton fabrics to the synergistic action of sunlight and existing levels of NO_x in the atmosphere during exposure.

An episode of runs in nylon stockings, which occurred in New York City, was traced to abnormal levels of NO_2 released during dynamite blasting operations. The combination of unfavorable weather conditions and NO_2 produced acid aerosols that damaged the nylon.

Nitrogen oxides react with Spandex, a synthetic elastomeric fiber, producing a yellow discoloration. This is an inherent property of the fiber rather than a dye-fading phenomenon.

High particulate nitrate levels have caused stress-corrosion failures of nickel-brass wire springs on relays used by telephone companies. Failures take place when surface nitrate concentrations exceed $2.4 \mu\text{g}/\text{cm}^2$ and the relative humidity is above 50 percent. This problem was first noticed in the Los Angeles area, where airborne nitrate levels are 5 to 15 times greater than in most eastern and midwestern cities in the United States.

Research on polymers suggests that atmospheric NO_2 may produce chain scission and crosslinking; nylon and some elastomers appear to be most sensitive.

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CHAPTER 7.

EFFECTS OF NITROGEN OXIDES ON VEGETATION

A. INTRODUCTION

The primary importance of nitrogen oxides (NO_x) as phytotoxicants was first inferred 20 years ago in California when photochemical oxidants were shown to have adverse effects on vegetation. The essential role of NO_x in the production of atmospheric oxidants, including peroxyacyl nitrates (PAN), and research activities in vegetative effects of these pollutants are reviewed in Air Quality Criteria for Photochemical Oxidants (1). Although the importance of NO_x in photochemical reactions is well recognized, the separate effects on vegetation attributable to the oxides of nitrogen per se are difficult to assess. Nevertheless, plant scientists agree that indirect exposure of sensitive plants to NO_x , through the photochemical reactions that produce oxidants, constitutes the most significant and widespread mechanism for NO_x phytotoxicity. These effects, however, have yet to be thoroughly examined.

Evidence of damage to plants resulting from direct exposure to NO_x in the atmosphere is usually confined to the proximity of specific industrial sources. For example, damage from high ambient levels of nitrogen dioxide (NO_2) has been observed near nitric acid plants. Direct damage by nitric oxide (NO) and other NO_x components or derivatives have not been delineated in the field.

In view of the foregoing, this chapter is limited to a discussion of the direct effects of NO_x on vegetation determined principally from the results of laboratory studies. The bulk of discussion is focused on the effects of NO_2 , but very recent, limited evidence of NO effects are also treated.

Plant response to phytotoxic levels of NO_x can be divided into three major categories: acute injury, chronic injury, and physiological effects. Acute injury is manifested by collapse of cells with subsequent development of identifiable necrotic patterns. Symptoms usually result from short exposures (hours) to varying levels of NO_2 , and appear within 2 to 48 hours after exposure.

Chronic injury is caused by intermittent exposure, over long periods, to low concentrations of gas. It results in chlorotic or other pigmented patterns in leaf tissue and may be accompanied by loss of leaves (leaf-drop)

Growth alterations, reduced yields, and changes in quality of plant products are among the physiological effects frequently associated with pollutant exposure. At present, atmospheric NO_x exposure has not been associated with any of these effects. In the laboratory physiological effects are often measured in terms of more subtle responses such as reduced photosynthesis or changes in rates of transpiration and enzymatic processes. Although most research concerning the physiological effects of NO_x has dealt with laboratory exposures to NO_2 , the effect of NO exposure has recently been measured in terms of

the reduction in apparent photosynthesis. Apparent photosynthesis is measured by the amount of carbon dioxide (CO_2) absorbed by the plant.

Descriptions of plant injury from NO_2 are found in two recent publications containing color plates (2,3).

B. ACUTE INJURY

Historically, vegetation in the vicinity of nitric acid plants has been injured by gases that escape during plant operations (4). Leaves develop brown or black spots, especially on the margins. The levels of exposure at which these effects become apparent are unknown, but probably vary widely. Experimental studies have not revealed any direct acute effect of NO exposure on vegetation.

Benedict and Breen (5) exposed 10 selected annual and perennial weeds to a mixture of NO and NO_2 for 4 hours. These plants were chosen as indicators of plant injury from air pollutants. Two types of markings developed: 1. a discoloration associated with collapse of cells and necrosis and 2. a general, overall waxy appearance of the leaf. With broad-leaved plants the collapsed, irregular-shaped necrotic markings were intercostal, but nearer the margins of the leaf. Middle-aged leaves usually developed the most markings; but with sunflower, annual bluegrass, and nettleleaf goosefoot, the middle-aged and old leaves were equally sensitive. On mustard plants, the oldest leaves were the most sensitive. In all species, the young leaves were injured least. Mustard was the most sensitive indicator tested, but all plants were somewhat resistant.

Heck (6) fumigated cotton, pinto bean, and endive plants with 1.9 mg/m^3 (1.0 ppm) NO_2 for 48 hours and observed slight, but definite, spotting on the leaves. When concentrations of 6.6 mg/m^3 (3.5 ppm) were used for 21 hours, mild necrotic spots appeared on cotton and bean; endive leaves were completely necrotic.

Van Haut and Stratmann (2) grouped plants in relation to their sensitivity or resistance to injury by NO_2 and NO . When 60 species of plants were fumigated with a 1:1 mixture of NO and NO_2 , they developed gray-green or brownish spots on the leaves, which later became necrotic. Leaf injury was similar to that caused by SO_2 , except that the nitrogen oxides were 2 to 5 times less toxic. Both very young and mature leaves were less sensitive than rapidly growing ones. The authors made no mention of duration or concentration of exposures.

MacLean et al. (7) exposed 14 ornamental species and 6 citrus varieties to high concentrations of NO_2 for short periods and classified them according to their susceptibility to injury. The fumigations caused marginal and intercostal necrosis, which was often visible within 1 hour. Collapsed tissues on the upper leaf surface suggested an initial injury to palisade cells. The necrosis later spread throughout the leaf. Citrus responded with the wilting of young leaves and leaf-drop. Older leaves developed marginal and intercostal necrosis. The varieties, listed in the order of decreasing sensitivity, were Marsh seedless grapefruit, pineapple orange, Valencia orange, Tangelo orange, Hamlin orange, and Temple orange. Ornamentals represented a wide range of

susceptibility. Tissue collapse and subsequent leaf-drop occurred rapidly in azaleas. Croton plants exposed to 282 mg/m^3 (150 ppm) for 4 hours showed slight intercostal necrosis, but Carissa given a like treatment showed no observable effects. Although defoliation and/or necrosis were complete in several instances, all species survived and axillary buds developed within 2 to 6 weeks.

C. CHRONIC INJURY

Evidence of chronic NO_x injury is limited. No evidence is available that would indicate a chronic effect of NO on plants. Leaf-drop and chlorosis were observed in navel orange trees after 35 days of fumigation with 0.94 mg/m^3 (0.5 ppm) NO_2 and leaf-drop after 8 months exposure to 0.47 mg/m^3 (0.25 ppm) (8). Similar effects were found on tobacco, tomato, spinach, and soybean plants exposed to the Los Angeles Basin smog; on the same plants raised in greenhouses equipped with carbon filters; and in irradiation chambers supplied with automobile exhaust from engines equipped with afterburners. Because leaf lesions typical of ozone injury were not observed, Glater postulated that low, constant levels of NO_x were the cause of injury (9).

D. PHYSIOLOGICAL EFFECTS

1. Observed Responses

Hill and Bennett (10) have compared the effect of NO with the effect of NO_2 on the rate of apparent photosynthesis of alfalfa and oats. A threshold concentration of about 0.7 mg/m^3 (0.6 ppm) NO or 1.1 mg/m^3 (0.6 ppm) NO_2 was required to reduce CO_2 assimilation. Combining the two gases gave an additive physiological effect. Nitric oxide

produced a more rapid reduction in apparent photosynthesis than NO_2 , and recovery was more rapid when the fumigation was stopped. Concentrations causing up to 50 percent reduction in apparent photosynthesis after 1 to 2 hours did not induce leaf injury.

Wellburn et al. (11) found that fumigation of leaves of broad bean with 1.88 mg/m^3 (1 ppm) of NO_2 for 1 hour caused swelling of the thylakoids within the chloroplasts; this swelling may explain reduction in photosynthesis. The effect was reversible.

Yields of the navel oranges exposed to 0.47 mg/m^3 (0.25 ppm) NO_2 for 8 months were reduced (8).

Taylor and Eaton (12) exposed pinto bean plants to 0.56 mg/m^3 (0.3 ppm) NO_2 for 10 to 19 days and reported a decrease in dry weight and an increase in unit-weight chlorophyll content. Similar studies with tomato plants exposed to concentrations ranging from 0.28 to 0.49 mg/m^3 (0.15 to 0.26 ppm) NO_2 showed a decrease in dry weight and leaf area, a darker green color, and a strong tendency for the leaves to curl downward.

Spierings (13) fumigated tomato plants during the entire growing season with 0.47 mg/m^3 (0.25 ppm) NO_2 and found that this resulted in a 22 percent decrease in crop yield.

2. Biochemical Mechanisms

Little work has been done on the biochemical mechanism(s) by which oxides of nitrogen cause direct injury to plants. When NO_2 reacts with water, it forms a stoichiometric mixture of nitrous and nitric acids. This reaction probably occurs as the gas reaches the wet surfaces of the spongy parenchyma in the leaves of plants. In vitro studies by Weill

and Caldwell (14) on the effect of 1 molar nitrous acid on beta-amylase from barley showed the enzyme to be slowly inactivated. They concluded that easily oxidized groups such as sulfhydryls could be affected. DiCarlo and Redfern (15) conducted more detailed studies with alpha-amylase obtained from Bacillus subtilis and concluded that the nitrite was reacting with an essential amino group in proteins. It reacts with two oxidation states of catalase, a hemoprotein from mammalian tissues, and with a peroxidase obtained from horseradish (16). These enzymatic studies have used one molar nitrite. This quantity is much higher than that which could be expected from exposure to atmospheric NO₂.

Spierings (13) observed the influence of prolonged NO₂ fumigation (0.25 ppm over the growing season) on the nitrogen metabolism of tomato plants grown in greenhouses. He found that the nitrogen content of the leaves was increased by the fumigation but that the nitrate content was lowered.

French investigators (17) exposed tomato and bean plants 8 hours per day for up to 5 days with a 1:1 mixture of NO and NO₂ at concentrations between 0.25 and 2.595 mg/m³ (0.16 to 1.67 ppm). Analysis of leaves showed that the concentration of total trichloroacetic acid (TCA) nitrogen was increased.

E. FACTORS AFFECTING RESPONSE TO NITROGEN DIOXIDE

Several factors such as species of plant, stage of plant development, plant environment (temperature, light, humidity, soil moisture, and mineral nutrition), and variable susceptibility within species (variety or

clone) influence the degree of injury to vegetation by air pollutants. Depending upon the kind of plant and its environment, one factor may be of much greater importance than another.

Benedict and Breen (5) reported that moist soil conditions caused several times as much injury to their ten test species as did dry conditions.

Taylor and MacLean (18) recognized the increased sensitivity of plants to NO_2 caused by low light intensity and reported that 5.6 mg/m^3 (3.0 ppm) NO_2 in darkness caused as much injury as 11.3 mg/m^3 (6.0 ppm) in light. Czech and Nothdurft (19), and van Haut and Stratmann (2) also reported that night fumigations may cause more injury than daytime exposures. Van Haut and Stratmann (2), reporting on the effect of time of day, found that NO_2 caused more leaf injury during certain periods than at others. Rye plants were more sensitive from 1200 to 1600 hr. Oats had a bimodal sensitivity, with more injury occurring from 2400 to 0200 hr than from 1200 to 1400 hr.

Of special interest are recent reports that show leaf injury occurring on tobacco after a 4-hour exposure to a mixture of 0.188 mg/m^3 (0.10 ppm) NO_2 and $260 \text{ } \mu\text{g/m}^3$ (0.10 ppm) SO_2 (20,21). If these pollutants act synergistically, perhaps low concentrations of each in combination with the other will cause plant injury.

F. DOSE-INJURY RELATIONSHIP BETWEEN NITROGEN DIOXIDE AIR POLLUTION AND VEGETATION

Dosage is a measure of the combination of duration of exposure and pollutant concentration; therefore, it is an essential element of air quality criteria. The general types of information needed and problems involved have been discussed in another air quality criteria document (1).

Presently, it is possible to cite only cursory results concerning the effects of variable dosages of NO_x on the physiology of plants (Table 7-1).

The acute effects of NO_2 have not been widely studied. In Table 7-2 the threshold injury level, which is defined as the exposure necessary to injure 5 percent of the area of the leaf (upper surface), is reported for various plants exposed to NO_2 . Preliminary time-concentration curves for several sensitivity groupings have been developed. Based on these curves, exposure durations and concentrations necessary to produce injury in sensitive, low-sensitive, and resistant plants at the threshold-injury level are indicated in Table 7-3. Table 7-4 gives a complete list of plants that have been studied, and places them in three NO_2 -susceptibility classes on the basis of the projections in Table 7-3.

Heck et al. (22) present a modified model for reporting injury to vegetation from a group of common air pollutants, including nitrogen dioxide. The model recognizes the separate influence of time and concentration and permits the development of a three-dimensional injury-response surface:

$$C = A_0 + A_1 I + A_2/T$$

where: C = Concentration, ppm
 A_0, A_1, A_2 = Constants (partial regression coefficients) specific for pollutant, plant species, and environmental conditions.
I = Percent injury
T = Time, hours

Constants developed for selected test species are shown in Table 7-5. These species are classed in susceptibility groupings based on projections in Table 7-3. The values of the constants are dependent upon

Table 7-1. CHRONIC INJURY BY AND PHYSIOLOGICAL EFFECTS OF NITRIC OXIDE AND NITROGEN DIOXIDE ON VEGETATION

Gas	Plant	Exposure			Effects	Reference
		Concentration,		Time, ^a days		
		ppm	mg/m ³			
NO	Gramineae Oat (<u>Avena sativa</u> , L.)	0.6	0.7	V	Reduced rate of apparent photosynthesis	11
	Leguminosae Alfalfa (<u>Medicago sativa</u> , L.)	0.6	0.7	V	Reduced rate of apparent photosynthesis	11
NO ₂	Gramineae Oat (<u>Avena sativa</u> , L.)	0.6	1.1	V	Reduced rate of apparent photosynthesis	11
	Leguminosae Alfalfa (<u>Medicago sativa</u> , L.)	0.6	1.1	V	Reduced rate of apparent photosynthesis	11
	Pinto Bean (<u>Phaseolus</u> <u>vulgaris</u> , L.)	0.3	0.6	10-19	Decrease in dry weight, increase in chlorophyll content per unit weight	13
	Broad Bean (<u>Vicia faba</u> , L.)	1.0	1.88	1/24th	Swelling of thylakoids in chloroplasts	12
	Rutaceae Navel orange (<u>Citrus</u> <u>sinensis</u> , Osbeck)	0.5-1.0	0.9-1.9	35	Chlorosis of leaves, extensive leaf-drop	8
		0.25	0.47	240	Increased leaf-drop, reduced yield	

Table 7-1. (Continued) CHRONIC INJURY BY AND PHYSIOLOGICAL EFFECTS OF NITRIC OXIDE AND NITROGEN DIOXIDE ON VEGETATION

Gas	Plant	Exposure		Time, ^a days	Effects	Reference
		Concentration,				
		ppm	mg/m ³			
Solanaceae Tomato (<u>Lycopersicon esculentum</u>)		0.15-0.26	0.3-0.5	10-22	Decrease in dry weight and leaf area, increase in chlorophyll, downward curvature of leaves	13
		0.25	0.47	130	Decrease in crop yield of 22%	14

^av = variable.

Table 7-2. PLANT THRESHOLD SUSCEPTIBILITY TO ACUTE INJURY FROM NITROGEN DIOXIDE

Species	Variety	Threshold			Effects ^a	Reference
		Concentration		Time, hr		
		ppm	mg/m ³			
Compositae						
Endive (<u>Cichorium endivia</u> , L.)	Ruffee	1	1.9	12	0	6
		1	1.9	48	1	6
Lettuce (<u>Lactuca sativa</u> , L.)		3.5	6.6	21	3	6
Mustard (<u>Brassica arvensis</u> , Rabenh.)	Ruby	4	7.5	1.5	1	22
Radish (<u>Raphanus sativus</u> , L.)	Cherry Belle	20	37.6	4	2	5
		5	9.4	0.5	1	22
Gramineae						
Oats (<u>Avena sativa</u> , L.)	329-80	4	7.5	1	1	22
Wheat (<u>Triticum vulgare</u> , Vill)	Wells	1	1.9	7	1	22
Leguminosae						
Alfalfa (<u>Medicago sativa</u> , L.)		30	56.4	1	1	19
Bean (<u>Phaseolus vulgaris</u> , L.)	Pinto	10	18.8	4	1	13
		1	1.9	12	0	6
		1	1.9	48	1	6
		3.5	6.6	21	1	6
Malvaceae						
Cotton (<u>Gossypium hirsutum</u> , L.)	Rex	1	1.9	12	0	6
		1	1.9	48	1	6
		3.5	6.6	21	1	6
	Paymaster	3	5.6	2	1	22
Cotton (<u>Gossypium</u> sp., L.)						
Solanaceae						
Tomato (<u>Lycopersicon esculentum</u> , Mill)	--	8	15	1	1	22
Tobacco (<u>Nicotiana glutinosa</u>)	--	2.4	4.5	5	0	13
		2.3	4.3	8.66	3	13

^aSeverity of injury: 1 = slight, 2 = moderate, and 3 = severe.

Table 7-3. PROJECTED NITROGEN DIOXIDE EXPOSURES FOR 5 PERCENT INJURY
LEVELS ON SELECTED VEGETATION^a

Time, hr	Concentrations producing injury					
	Sensitive, ^b		Low-sensitive,		Resistant,	
	ppm	mg/m ³	ppm	mg/m ³	ppm	mg/m ³
0.5	6-10	11.3-18.8	9-17	16.9-32.0	≥16	≥30.1
1.0	4-8	7.5-15.0	7-14	13.1-26.3	≥13	≥24.4
2.0	3-7	5.6-13.2	6-12	11.3-22.6	≥11	≥20.7
4.0	2-6	3.8-11.3	5-10	9.4-18.8	≥ 9	≥16.9
8.0	2-5	3.8- 9.4	4-9	7.5-16.9	≥ 8	≥15.0

^aReference 22.

^bPlant type.

Table 7-4. RELATIVE PLANT SENSITIVITY TO NITROGEN DIOXIDE INJURY

Species	Variety	Reference
<u>Sensitive plants</u>		
Apocynaceae		
Periwinkle (<u>Vinca minor</u> , L.)	Bright Eyes	22
Balsaminaceae		
Sultana (<u>Impatiens sultani</u> , Hook.)	White Impatiens	22
Begoniaceae		
Begonia (<u>Begonia Rex</u> , Putz.)	Thousand Wonders White	22
Compositae		
Chrysanthemum (<u>Chrysanthemum</u> , sp.)	Oregon	22
Cruciferae		
Broccoli (<u>Brassica oleracea botrytis</u> , L.)	Calabrese	22
Radish (<u>Raphanus sativus</u> , L.)	Cherry Belle	22
Gramineae		
Bromegrass (<u>Bromus inermis</u> , L.)	Sac Smooth	22
Oats (<u>Avena Sativa</u> , L.)	Clintland 64	22
	329-80	22
	Pendek	22
Wheat (<u>Triticum vulgare</u> , V.11.)	Wells	22
<u>Low-sensitive plants</u>		
Leguminosae		
Bean (<u>Phaseolus vulgaris</u> , L.)	Pinto	13
Soybean (<u>Glycine max</u> , Merr.)	Scott	22
Malvaceae		
Cotton (<u>Gossypium hirsutum</u> , L.)	Acala 4-42	22
Solanaceae		
Tobacco (<u>Nicotiana tabacum</u> , L.)	White Gold	22
	Bel - B	22
	Beltsville W3	22

Table 7-4. (Continued) RELATIVE PLANT SENSITIVITY TO NITROGEN DIOXIDE INJURY

Species	Variety	Reference
<u>Tomato (Lycopersicon esculentum, Mill.)</u>	Roma	22
<u>Resistant plants</u>		
<u>Amaranthaceae</u>		
<u>Pigweed (Amaranthus retroflexus)</u>	--	5
<u>Caryophyllaceae</u>		
<u>Chickweed (Stellaria media, Cyrill)</u>	--	5
<u>Chenopodiaceae</u>		
<u>Beet (Beta vulgaris, L.)</u>	Perfected Detroit	22
<u>Lamb's-quarters (Chenopodium album, L.)</u>		5
<u>Nettle-leaf goosefoot (Chenopodium murale)</u>		5
<u>Compositae</u>		
<u>Dandelion (Taraxacum officinale, Weber)</u>	--	5
<u>Sunflower (Helianthus annuus, C.)</u>	--	5
<u>Cucurbitaceae</u>		
<u>Cucumber (Cucumis salivus, L.)</u>	Long Marketeer	22
<u>Ericaceae</u>		
<u>Azalea (Rhododendron, sp.)</u>	Alaska	22
<u>Euphorbiaceae</u>		
<u>Croton (Codiaeum, Juss)</u>	--	7
<u>Gramineae</u>		
<u>Annual bluegrass (Poa annua, L.)</u>	--	5
<u>Corn (Zea mays, L.)</u>	Pioneer 509-W	22
	Golden Cross	22
<u>Kentucky bluegrass (Poa pratensis)</u>		5
<u>Orchard grass (Dactylis glomerata, L.)</u>	Potomac	22
<u>Sorghum (Sorghum, sp.)</u>	Martin	22
<u>Malvaceae</u>		
<u>Cheeseweed (Malva parviflora, L.)</u>	--	5

Table 7-4. (Continued) RELATIVE PLANT SENSITIVITY TO NITROGEN DIOXIDE INJURY

Species	Variety	Reference
Solanaceae Tobacco (<u>Nicotiana tabacum</u> , L.)	Beltsville B W3 Burley 21	22 22 22

Table 7-5. NITROGEN DIOXIDE TIME-CONCENTRATION RESPONSE EQUATIONS
(0.5 to 7 hours)^a (22)

$$C = A_0 + A_1 I + A_2/T$$

Species	A ₀	A ₁	A ₂	R ²	D	E	D+E
Sensitive plants							
Oats (Clintland 64)	1.45	0.13	24	0.76	4.5	2.3	6.8
Radish (Cherry Belle)	2.40	0.14	1.02	0.83	4.1	3.2	7.3
Oats (329-80)	1.75	0.15	3.24	0.56	5.7	2.9	8.6
Bromegrass (Sac Smooth)	2.49	0.16	1.9	0.71	5.2	3.5	8.7
Begonia	2.45	0.15	2.99	0.63	6.2	3.5	9.7
Chrysanthemum	3.16	0.16	2.14	0.72	6.1	3.7	9.8
Oats (Pendek)	2.79	0.14	2.88	0.50	6.4	3.8	10.2
Wheat (Wells)	2.80	0.13	2.94	0.52	6.4	3.8	10.2
Sultana	3.93	0.13	1.73	0.67	6.3	4.8	11.1
Broccoli	3.07	0.20	2.94	0.53	7.0	4.5	11.5
Periwinkle	2.92	0.23	3.02	0.55	7.1	4.5	11.6
Low-sensitive plants							
Cotton (Paymaster)	3.97	0.23	1.94	0.58	7.1	5.3	12.4
Cotton (Acala 4-42)	3.68	0.22	3.15	0.50	7.9	5.2	13.1
Tobacco (Bel B)	3.62	0.21	3.98	0.38	8.7	5.2	13.9
Tobacco (Bel W ₃)	3.65	0.18	4.40	0.31	9.0	5.2	14.2
Tobacco (White Gold)	4.03	0.30	3.56	0.40	9.1	6.0	15.1
Resistant plants							
Tobacco (Burley 21)	1 of 36 plants injured; 0.5 hr, 26 ppm, 33 percent						
Corn (Pioneer 509-W)	4 of 36 plants injured; All injuries were 1.6 percent						
Corn (Golden Cross)	1 of 36 plants injured; 7.0 hr, 6 ppm, 7 percent						
Azalea (Alaska)	1 of 36 plants injured; 1.0 hr, 17 ppm, 5 percent						
Sorghum (Martin)	0 of 36 plants injured						
Cucumber (Long Marketeer)	0 of 36 plants injured						

^a See text for explanation of equation.

R² = Coefficients of determination; represent percent variation in model.

D = Concentrations that will cause 5 percent injury in 1 hour.

E = Concentrations that will cause 5 percent injury in 8 hours.

D+E = Basis for placing the plant in a specific susceptibility category; exact cut-off sums not yet established.

the prevailing environmental conditions. The experimental design suggests that these equations can be used by control agencies to predict injury to vegetation under environmental conditions when vegetation would be most sensitive (high humidity and temperatures between 24 and 32 °C). These equations are preliminary attempts to place usable tools in the hands of control agencies. The equations should not be applied to time periods less than 30 minutes or more than 8 hours, or for concentration averages below 0.5 ppm or above 25.0 ppm.

G. FUTURE RESEARCH

Plants vary in sensitivity to NO_x . Further testing in the high concentration range [28 to 47 mg/m^3 (15 to 25 ppm)] for more than 1 hour will yield little more information, except to show the exact kind of leaf lesions that will occur on a given species. This information would only be worthwhile for evaluating injury caused by large-scale spillage, by rocket fuel ignition, by accidental release of concentrated gas, or by elevated atmospheric levels in the vicinity of poorly controlled industries that use or produce NO_2 .

Much time and effort must be expended in determining in detail how lower levels of NO_x affect vegetation. Representative species must be grown under a variety of carefully controlled, reproducible, environmental conditions. The plants selected as standards would then have to be fumigated with specific concentrations of NO_2 and/or NO for specified times.

Evaluation would require preliminary in vitro work to determine the effect of NO_x gases on enzymes, growth regulators, plant pigments, and

other metabolic systems. Selected fractions of treated plants and untreated, but similarly grown, controls could then be analyzed for the same reactions. Enzymatic effects should be pursued intensively to define the way in which the particular pollutant affects plant metabolism. As biochemical effects are understood, correlations can be made with reactions known to occur in other organisms such as mammals, insects, and birds.

The tentative findings by Tingey et al. (21) involving synergism show that studies should be broadened to explore more fully the interactions between NO_x and other air pollutants.

H. SUMMARY

Many kinds of plants develop severe acute leaf injury (lesions) when exposed to concentrations of NO_2 greater than 47 mg/m^3 (25 ppm) for a 1-hour period. Though characteristic for each plant, the lesions are difficult to distinguish from similar injury caused by SO_2 . The fact that both very young and mature leaves are more resistant to NO_2 than are those that are expanding rapidly may provide aid in identifying NO_2 injury.

Under controlled growth conditions, the injury-threshold value for NO_2 (the level that injures 5 percent of the leaf area) for certain sensitive plants is 7.5 to 15.0 mg/m^3 (4 to 8 ppm) for 1 hour. Increasing the duration of exposure decreases the injury threshold value; for example, NO_2 concentrations of 4.3 to 6.6 mg/m^3 (2.3 to 3.5 ppm) for 8 to 21 hours or concentrations of 1.9 mg/m^3 (1 ppm) for 48 hours cause leaf injury to sensitive plant species. Continuous fumigation with 0.94 mg/m^3 (0.5 ppm) NO_2 for 35 days resulted in leaf drop and chlorosis in citrus, but no actual necrotic lesions developed.

The effects of exposure to low levels of NO_2 for extended periods are less evident. Recently completed studies suggest that 0.47 mg/m^3 (0.25 ppm) or less of NO_2 supplied continuously for 8 months increased leaf-drop and reduced yield of navel oranges. A 4-month exposure to 0.47 mg/m^3 (0.25 ppm) NO_2 resulted in a 22 percent reduced yield of tomatoes. The degree of injury from lower, atmospheric concentrations of NO_2 remains to be determined. Decreased weight of leaves resulted from fumigation of pinto bean plants with 0.56 mg/m^3 (0.3 ppm) and of tomato plants with 0.28 to 0.49 mg/m^3 (0.15 to 0.26 ppm) NO_2 . These conditions approximate the possible effects of persistently high ambient concentrations.

The limited information on the effectiveness of NO in reducing apparent photosynthesis indicates that it would reduce the growth of plants if concentrations in the range of 3.8 to 7.5 mg/m^3 (2 to 4 ppm) persisted continuously.

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CHAPTER 8.

TOXICOLOGICAL EFFECTS OF NITROGEN OXIDES

A. INTRODUCTION

The toxicological effects of oxides of nitrogen (NO_x) have been studied extensively through animal experiments and accidental exposures of human beings. Additionally, a few experimental exposures to nitrogen dioxide (NO_2) have been carried out in human volunteers. Because of their slight solubility in water, nitric oxide (NO) and NO_2 penetrate deeply into the respiratory tract and reach the alveoli. The absorption of both gases is virtually the same: during normal respiration, over 80 percent of the nitrogen oxides is retained in the respiratory tract (1).

Animal mortality studies indicate that NO_2 is about four times more toxic than NO (2). This chapter represents an attempt to evaluate studies on the health effects of NO and NO_2 and to identify the probable hazardous doses of both pollutants.

B. NITRIC OXIDE

No cases of human poisoning from NO have been reported in the scientific literature, although NO is undoubtedly present in occupational exposures to NO_x . When present in high concentrations, NO is rapidly converted to NO_2 , a property that makes it difficult to control NO concentrations in laboratory experiments.

In animals, extremely high concentrations of NO produced central nervous system paralysis and convulsions (3). Mice exposed to 3075 mg/m^3 (2500 ppm) were narcotized in 6 to 7 minutes and died within 12

minutes, but if the narcotized animals were returned to fresh air after 4 to 6 minutes of exposure, they recovered rapidly.

Data from limited experiments on guinea pigs indicate no effect on pulmonary function from 4-hour exposures to concentrations of 19.7 to 94.0 mg/m³ (16 to 50 ppm) NO (4).

1. Methemoglobin Increase

Methemoglobin (MeHb) does not bind oxygen; hence, it reduces the oxygen-carrying capacity of blood when it replaces normal hemoglobin (Hb). Low concentrations of MeHb, ranging from 0.01 to 0.5 gram MeHb per 100 milliliters (g/100 ml), are usually present in normal human blood (5), although the range in normal subjects has been reported to vary between 0 and 8 percent of total hemoglobin (6), i.e., up to 1.2 g MeHb/100 ml, when the hemoglobin value is 15 g/100 ml. The earliest clinical evidence of MeHb in human blood is cyanosis, which begins when the MeHb concentration reaches 10 to 15 percent of the total Hb, a concentration not likely to result from exposure to ambient concentrations of NO_x. Symptoms such as exertional dyspnea (labored breathing), which reflects hypoxia (low oxygen supply), are not likely to appear until blood levels of MeHb reach 30 to 45 percent of total Hb (5).

High quantities of MeHb and cyanosis were detected in the blood of animals that died as a result of poisoning from exposures to 1500 mg/m³ (1200 ppm) NO (7,8). The threshold NO concentration for MeHb formation, as measured in arterial blood of Wistar rats, lies between 5 and 10 ppm. No evidence for MeHb formation could be found at 5 ppm NO in an acute exposure of 60 minutes. A concentration of 10 ppm NO caused an increase

of more than 50 percent over the initial MeHb value. Post-exposure recovery was nearly completed within an hour (9).

Evidence concerning MeHb formation following exposure to lower concentrations of NO is conflicting.

The significance of low blood levels of MeHb is not well understood. In Chapter 9, the use of blood levels of MeHb as an index of exposure to ambient NO_x is discussed (10), but few epidemiological investigators actually use this parameter in their experimental design.

In vitro, NO combines with hemoglobin to form NO-hemoglobin (NO-Hb) and with MeHb to form NO-methemoglobin (NO-MeHb), both of which have biological half-lives of about 2 days. A preliminary examination, using electron-spin resonance, of the blood of rats exposed for 1 and 9 days to 12.3 mg/m³ (10 ppm) NO in air revealed neither NO-Hb nor NO-MeHb (11).

2. Enzyme Inhibition

A concentration of about 24.6 mg/m³ (20 ppm) NO inhibited hydrogenase activity of the bacterium Proteus vulgaris, both in vivo and in vitro (12). This activity could be restored by the addition of Na₂S₂O₄, which reduced NO to nitrous oxide (N₂O), except at concentrations of 12,300 mg/m³ (10,000 ppm) NO and above, where inhibition was irreversible.

Although ambient levels of NO are not inherently toxic, the toxicological potential of NO lies in its relationship to NO₂, which is discussed elsewhere (13).

C. NITROGEN DIOXIDE

1. Effects in Animals

a. Mortality

Many early studies produced negative evidence of NO₂ toxicity in

animals. This may have resulted from the presence of large amounts of NO in the experimental mixtures, for recent studies have produced more reliable and positive evidence of toxicity. Several factors affecting the mortality attributable to NO₂ are discussed in the following section.

1) Length of exposure and concentration. Short exposures of rats to high concentrations are more toxic than equivalent exposures to low concentrations for longer times. This is illustrated in Table 8-1.

Most investigations involving inhalation of high concentrations of NO₂ have implicated pulmonary edema as the major cause of death. When

Table 8-1. COMPARISON OF LETHAL LEVELS OF ACUTE
EXPOSURE OF MALE RATS TO NO₂ (14)

Number of experiments	Exposure time, min	LC ₅₀ ^{a,b}		LCT ₅₀ ^{b,c}
		ppm	mg/m ³	ppm x min
3	2	1,445 ^d	2,715	2,890
2	5	833 ^d	1,566	4,165
6	15	420(362-487)	790(680-916)	6,300(5,430-7,305)
10	30	174(154-197)	325(290-370)	5,220(4,620-5,910)
10	60	168(153-185)	315(290-350)	10,080(9,180-11,100)
7	240	88 (79-99)	165(140-185)	21,120(18,960-23,760)

^aLC₅₀ represents the concentration lethal to 50 percent of the animals.

^b95 percent confidence limits in parenthesis.

^cLCT₅₀ represents the exposure (concentration x time) lethal to 50 percent of the animals.

^dNo confidence limits.

112 animals of various species were exposed to 56.4 to 1880 mg/m³ (30 to 1000 ppm) NO₂, 84 animals died - 74 from pulmonary edema, 5 from asphyxia, and 5 from pneumonitis (inflammation of lung tissues) (Table 8-2). Exposure to 56.4 mg/m³ (30 ppm) NO₂ for 3 hours produced no apparent immediate or delayed harmful effects in guinea pigs. The harmful effects of 2- to 3-hour exposures of 103.4 mg/m³ (55 ppm) NO₂ were questionable in experiments with rats and mice. None were found at the same concentration with rabbits, cats, and guinea pigs (15).

It is rare that any species can withstand exposure to NO₂ concentrations of 188 to 1880 mg/m³ (100 to 1000 ppm). In experiments with these concentrations, death occurred after 10 minutes to 21 hours of exposure, depending on the animal (14). Exposure for 4 hours to 99.6 mg/m³ (53 ppm) NO₂ was fatal to rats; exposure for 4 hours to 122.2 to 141 mg/m³ (65 to 75 ppm) NO₂ was fatal to dogs.

Table 8-2. TIME NECESSARY TO PRODUCE DEATH IN ANIMALS^a
EXPOSED TO HIGH CONCENTRATIONS OF NO₂ (15)

Concentration		Time until death, min	% deaths
ppm	mg/m ³		
30	56.4	---	0
100	188.0	318	74
150	282.0	90	70
400	752.0	58	92
600	1,128.0	32	93
800	1,524.0	29	100
1,000	1,880.0	19	100

^aAnimals included the following species: cats, guinea pigs, mice, rats, and rabbits. Death occurred in 84 of 112 animals.

- 2) Temperature. An ambient temperature increase of about 11°C (20°F) increases the toxicity of NO₂ for rats by about 25 percent (16).
- 3) Presence of other irritants. The survival time for rabbits was increased from 60 to 140 minutes when nonlethal amounts of sulfur dioxide (SO₂) were added to the NO₂ dose that caused 50 percent mortality (16).

b. Respiratory Tract Effects

- 1) Changes in pulmonary function. Short-term (less than 4 hours) exposure to NO₂ produced reversible changes in pulmonary function in animals (4,17). In general, both short-term and continuous exposures caused respiratory rates to increase and tidal volumes (the volume of air inhaled in an average single breath) to decrease during exposures to concentrations of NO₂ ranging from 1.5 (0.8 ppm) to 94 mg/m³ (50 ppm). The degree of response varied with the exposure and the animal (Table 8-3 and Figure 8-1).

Other pulmonary functions have been examined, but show no evidence of being affected by NO₂. Guinea pigs exposed to 9.4 mg/m³ (5 ppm) NO₂ for either 4 or 7.5 hours a day, 5 days a week, for periods up to 5.5 months, had no changes in expiratory flow resistance (18). Four rabbits exposed to 47.0 mg/m³ (25 ppm) NO₂ continuously for 18 months had a transient increase in the rate of oxygen consumption. The rate reverted to normal within 48 to 72 hours after exposure. In 16 rabbits exposed to 1.9 and 9.4 mg/m³ (1 and 5 ppm) NO₂ for the same length of time, no change in oxygen consumption occurred (19).

Beagles exposed to 0.9 to 1.9 mg/m³ (0.5 to 1.0 ppm) NO₂ plus 245 µg/m³ (0.2 ppm) NO, and to 2.8 to 3.8 mg/m³ (1.5 to 2.0 ppm) NO₂ plus 245 µg/m³ (0.2 ppm) NO, for 16 hours a day for 18 months, showed no

Table 8-3. CHANGES IN PULMONARY FUNCTION IN ANIMALS EXPOSED TO SUBLETHAL DOSES OF NO₂

Animal	Concentration		Exposure time	Respiratory rate	Tidal volume	Minute volume	Time for maximum effect, min	Recovery		References
	mg/m ³	ppm						Amount	Time	
Guinea pigs	9.8 12.2 16.9 24.4	5.2 6.5 9.0 13.0	2 to 4 hr	^a	---	0	180 135 90 60		Within 4 hr	4
Squirrel monkeys (<u>Saimiri sciureus</u>)	18.8 and 28.2	10 and 15	2 hr	0	---	---	n.a.	complete	24-48 hr	17
	65.8 and 94.0	35 and 50	2 hr	++	---	n.a.	n.a.	complete	Up to 72 hr	
Rats	1.5	0.8	continuous, lifetime	+(20%)	n.a.	n.a.	n.a.	none	Lifetime	94
Monkeys (<u>M. speciosa</u>)	3.8 and 16.9	2 and 9	continuous	±	---	n.a.	n.a.	none	2 yr	45
Squirrel monkeys (<u>Saimiri sciureus</u>)	9.4 18.8	5 10	2 mo 1 mo	+	---	0	n.a.	n.a.		71
				+	+	+	n.a.	n.a.		
Rabbits	94 75 56	30 40 50	15 min	Diminishes diffusion			n.a.	n.a.		21

^aKey: + = Increased; - = decreased; 0 = unchanged; n.a. = not available.

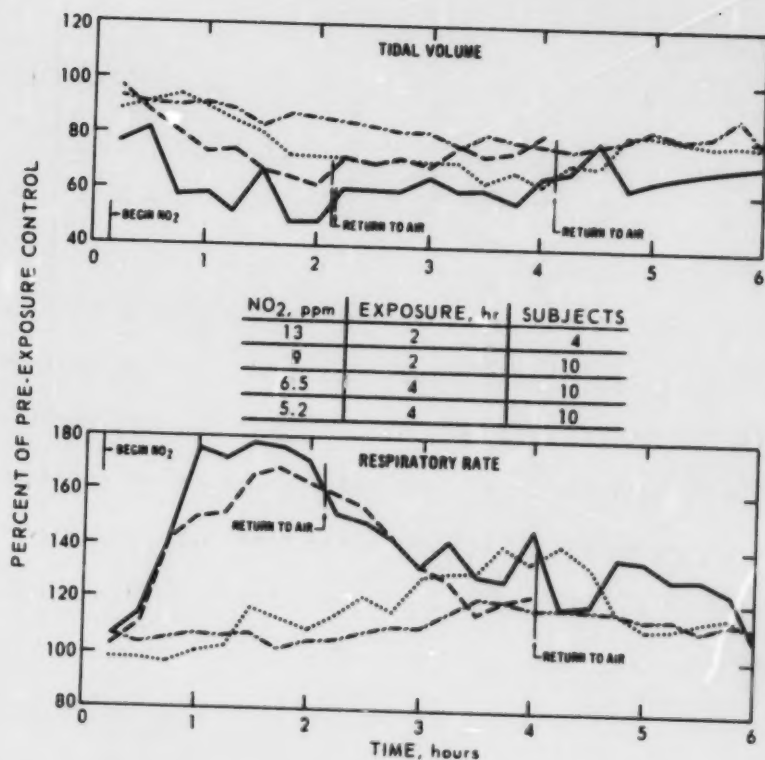


Figure 8-1. Effect of NO₂ on tidal volume and respiratory rate of guinea pigs (4).

changes in body weight, in carbon monoxide (CO)-diffusing capacity, compliance, or total expiratory resistance of the lungs when compared with a control group of 20 beagles breathing filtered air (20).

Concentrations of 94, 75, and 56 mg/m³ (50, 40, and 30 ppm) NO₂ inhaled for 15 minutes caused a marked change (decrease) in the perfusion - distribution in the lungs of rabbits in vivo as measured by radio labeled isotopes (21).

While the data from the above experiments are derived from exposure to concentrations of NO₂ that are not relevant to air pollution, data given below on experimentally exposed human beings indicate that diffusion changes can result from exposure to much lower concentrations.

2) Chemical effects.

a) Structural proteins--Nitrogen dioxide can alter the configuration of the lung tissue structural proteins, collagen and elastin (22). One animal from each of five sets of four litter-mate female rabbits served as a control; one breathed 1.9 mg/m^3 (1 ppm) NO_2 for 1 hour and the remaining two breathed 9.4 mg/m^3 (5 ppm) NO_2 for 1 hour. All the animals were sacrificed immediately after exposure, except one in the last group, which was sacrificed 24 hours after exposure. The lungs were excised and converted to a lipid-free powder from which collagen and elastin were isolated by a combination of solvent extraction and enzymatic hydrolysis. Differential ultraviolet spectrophotometry indicated that the molecular structures of both collagen and elastin were altered in both exposure groups. Similarities between the spectra of collagen and elastin from the animal sacrificed 24 hours after exposure and those from the control animal indicated that the changes were reversible under the conditions of the experiment. The authors suggested that the metabolic activity of lung tissue may have been reduced in the highly acidic environment produced by exposure to NO_2 and speculated that repeated exposure to NO_2 with concurrent repeated denaturation of collagen and elastin may be a factor in the etiology of pulmonary emphysema.

Rabbits exposed to $470 \text{ } \mu\text{g/m}^3$ (0.25 ppm) NO_2 , 4 hours a day for 6 days, and sacrificed immediately, developed structural changes in the lung collagen, as determined by electron microscopy. These changes were not reversible and were apparent in animals sacrificed 7 days after the final exposure (23). Data suggesting denaturation of pulmonary connective tissue may be extremely relevant in view of the experimental

production of pulmonary emphysema by NO_2 exposure by a number of workers (See below).

b) Lipid peroxidation--Short-term low-level exposures for 4 hours to 1.9 mg/m^3 (1 ppm) produced evident peroxidation in extracts of lipids from rat lungs (24). Peroxidation was maximal 24 hours after exposure, and lasted for at least another 24 hours. In six daily 4-hour exposures to 1.9 mg/m^3 (1 ppm), lipid peroxidation increased, possibly as a cumulative effect. The significance of this peroxidation has not yet been established; however, rats fed a vitamin-E-deficient diet and exposed to NO_2 had more peroxidation in both surfactant and tissue lipids than did those on vitamin-E-supplemented diets (25). (Vitamin E is an antioxidant.)

c) Perfused lung. Isolated rabbit lungs were perfused with a dextrane solution and artificially ventilated. After a stabilization period of 60 minutes, NO_2 was added to the air at concentrations of 94 and $38 \text{ } \mu\text{g/m}^3$ (50 and 20 ppm). The release of enzymes [lactate dehydrogenase (LDH) and malate dehydrogenase (MDH)] from the lungs into the dextran solution was measured during the whole course of the experiment. A significant increase in enzyme activity was observed in the perfusion fluid immediately after the initiation of the NO_2 exposure (Figure 8-2). The rate of increase was the same for both enzymes. The controls did not show this constant increase (see Figure 8-2) (26). Because enzyme activity of MDH and LDH expressed in absolute units differed greatly, relative activity was chosen to show the identical rates of increase. Enzyme activity immediately before NO_2 exposure was taken as 100 percent.

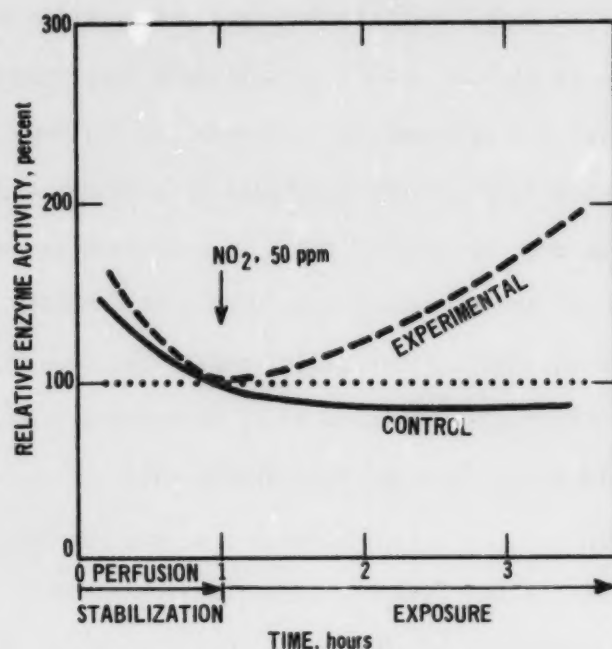


Figure 8-2. Effects of 50 ppm NO_2 on malate dehydrogenase (MDH) and lactate dehydrogenase (LDH) in rabbit lung perfused with dextran

3) General Pathological Effects. Pathologically, all animal lungs demonstrate the same general pattern of response to NO_2 irrespective of the duration of exposure, but the severity of response tends to increase as the concentration increases. An inflammatory reaction, characterized by macrophage infiltration and epithelial degeneration, occurs during the 24-hour period immediately following exposure and can develop into pulmonary edema in the presence of sufficiently high NO_2 concentrations. Subsequent regeneration follows. Such changes have been observed in rabbits exposed to 188 mg/m^3 (100 ppm) and in rats and guinea pigs exposed to 141 to 150 mg/m^3 (75 to 80 ppm) NO_2 for 2 hours (27). In experiments in which rats and guinea pigs were exposed to 28.2 to 37.6 mg/m^3 (15 to 20 ppm) and rabbits to 47.0 mg/m^3 (25 ppm) NO_2 for 2 hours

a day for 5 successive days, initial edema and inflammation were not as severe as they were in animals used in single-dose experiments; however, chronic peribronchial and perivascular inflammation followed later. On the fourth day after epithelium was destroyed by a single high dose of NO_2 , lung tissue was seen to repair itself in both rabbits and guinea pigs. Regeneration became rapid and appeared to be complete in 2 weeks. After a series of high intermittent doses, repair was slower; animals exposed intermittently during a period of 21 months required up to 3 weeks after the last exposure for recovery (27,28).

4) Cellular Changes.

a) Structural damage--short-term exposure--In short-term exposures to low concentrations [0.9 mg/m^3 (0.5 ppm) for 4 hours or 1.9 mg/m^3 (1 ppm) for 1 hour] of NO_2 , rats sustained reversible lung tissue change (29). In tissues from animals sacrificed immediately after exposure, the mast cells were ruptured and disoriented, and showed loss of cytoplasmic granules. This occurred primarily in the pleura, bronchi, and surrounding tissues, but most markedly in the mediastinum. This response seemed reversible, since animals sacrificed 24 to 27 hours after exposure appeared to have only a few ruptured mast cells. The investigators believed that the release of granular material from the lung mast cells in response to NO_2 inhalation signified the onset of an acute inflammatory reaction.

After 4 hours of exposure to 32.0 mg/m^3 (17 ppm) NO_2 , the appearance of bits of free fibrin in both alveolar spaces and tissue indicated transient leakage of plasma from rat alveolar capillaries. As exposure continued in the same experiment, focal injury to type I alveolar

epithelial cells became exaggerated by 48 hours, as indicated by bits of amorphous cellular debris in ductal alveoli. The facts that fibrin and debris tended to disappear and that injured cells healed as exposure continued suggests the development of tolerance (30). A single 6-hour exposure to NO_2 in concentrations ranging from 75.2 to as low as 4.7 mg/m^3 (40 to as low as 2.5 ppm) significantly increased the LD_{50} for rats and mice when later, they were continuously exposed to higher concentrations of NO_2 . This is another indication of tolerance formation (31,32). Cellular alteration in the terminal airways was noted after exposure to 3.8 mg/m^3 (2 ppm) NO_2 for 72 hours. This was followed by a recovery phase that was fairly complete by 21 days of continuous exposure at the same concentration. This adaptive reaction to low-level NO_2 exposure is of great interest and probably represents the earliest epithelial reaction in the dose response (33).

Cell renewal in the lungs following exposure to NO_2 has been studied by measuring the uptake of tritiated thymidine by dividing cells. Striking differences in thymidine uptake between controls and animals exposed to 31.9 mg/m^3 (17 ppm) NO_2 , and less marked but statistically significant increases, were noted after exposure to 3.8 mg/m^3 (2 ppm) NO_2 . These changes began the first day of exposure, peaked at 2 days following onset of exposure, and returned to baseline levels by 6 days.

The increase in cell division in the terminal bronchiole was associated with development of increased cell division in alveoli adjacent to the ends of the terminal bronchioles, and presumably was the result of replacement of damaged epithelial cells. The authors suggest that the cuboidal cell hyperplasia in these affected alveoli

result from replacement of damaged type I cells by proliferating type II cells. These changes apparently represent initial cellular injury followed by replacement through the formation of new cells within a few days after the onset of exposure to NO_2 . It is of interest to note that such cellular mitotic activity takes place while exposure is continuing and that this represents an adaptive change (34).

Primary lesions appeared in lung alveoli of squirrel monkeys exposed for 2 hours to 18.8 to 94.0 mg/m^3 (10 to 50 ppm) NO_2 . Progressive alveolar expansion occurred with increasing concentrations of NO_2 . At 18.8 mg/m^3 (10 ppm) NO_2 , many septal breaks appeared and the alveoli expanded markedly. In some areas, large air vesicles with extremely thin septal walls were seen. Other tissues appeared to be normal. At 28.2 mg/m^3 (15 ppm) NO_2 , alveolar tissue was expanded with minimal wall thinning and patchy interstitial infiltration with lymphocytes. The bronchioles were normal. At 65.8 mg/m^3 (35 ppm) NO_2 , areas of lung were collapsed and alveolar septa became highly basophilic. In other areas, the alveoli were expanded and had thin septal walls. The bronchi were moderately inflamed; some showed epithelial proliferation (17). Exposure to 94.0 mg/m^3 (50 ppm) NO_2 resulted in extreme vesicular dilatation or total collapse of alveoli, along with extensive edema and lymphocytic infiltration. The bronchi showed epithelial surface erosion and absence of cilia.

b) Orientation changes--continuous exposure--After 3 days of continuous exposure to 3.8 mg/m^3 (2 ppm) NO_2 , the terminal bronchiolar epithelium of rats changed from an active, nonhomogeneous layer to a uniform layer of enlarged cells. This subtle biological effect of NO_2 on epithelial cell metabolism was further documented by the demonstration

of abnormal ciliogenesis. Although ciliary basal bodies developed normally, they failed to orient appropriately at the apical surfaces of the cells. They either formed no cilia or directed them intracytoplasmically into vacuoles. Intracytoplasmic, crystalloid inclusion bodies also developed in time (30,35,36).

c) Hyperplasia--In another case, continuous exposure to 32.0 mg/m^3 (17 ppm) NO_2 precipitated a wave of accelerated cellular replication (hyperplasia) of terminal bronchiolar and type II epithelial cells and macrophages in rat lungs. This response was measured both by nuclear autoradiography of tritiated thymidine incorporation and by mitotic-figure counts (37). The activity peaked at 24 hours after exposure began and returned to baseline values within a week, despite the continued exposure, and was without apparent vital injury to the epithelial cells involved.

In hamsters continuously exposed to higher NO_2 concentrations 84.6 to 103.4 mg/m^3 (45 to 55 ppm) for 2.5 months, researchers noted transitory hyperplasia of the respiratory bronchiolar epithelium. The lung volumes increased during exposure but reverted toward normal after a 2-week recovery period (38). In hamsters exposed to 188 mg/m^3 (100 ppm) NO_2 for 6 hours, tritiated thymidine uptake indicated intense epithelial proliferation in the major bronchi that was maximal 24 hours after exposure and normal again within 4 days after exposure ended. In the peripheral bronchi, cellular proliferation was delayed and less intense (39).

d) Emphysematous lesions--With exposures of 3 months or longer, 0.9 to 47.0 mg/m^3 (0.5 to 25 ppm) NO_2 caused changes in animal lung tissue similar to those seen in human emphysema. Pre-emphysematous lesions

indicative of the development of early focal emphysema were observed in the lungs of mice exposed to $940 \mu\text{g}/\text{m}^3$ (0.5 ppm) NO_2 for 6, 18, and 24 hours a day for periods from 3 to 12 months (Table 8-4) (40).

Alveoli consistently increased in size by cell distension rather than by septal breakage. The investigators in this study also noted inflammation of the bronchiolar epithelium and reduction in distal airway size.

Continuous exposure of young rats to 18.8 to $47.0 \text{ mg}/\text{m}^3$ (10 to 25 ppm) NO_2 produced voluminous, heavy, dry, air-retaining lungs in expanded, kyphotic thoraces--a condition grossly resembling emphysema (see Table 8-5) (41-44). Such animals died of respiratory complications after several months of exposure. Pathological findings included narrow, occasionally fibrotic and occluded terminal bronchioles with no cilia; distended, ruptured peripheral alveoli; and alterations in the staining characteristics of both collagen and elastic tissue, particularly in tissue from the alveolar ducts (45). Terminal bronchiolar, ductal, and adjacent alveolar epithelium was hypertrophic (enlarged).

When animals so exposed were allowed to recover, the hypertrophic epithelium of the lungs receded and cilia reappeared. With the recession, the lung weights returned to normal. Additional pulmonary connective tissue usually appears in rats as a part of aging; however, the previously exposed, healing rats developed lungs of excessive weight compared with controls of the same age. This suggested an anamnestic connective-tissue response in old age (46). Abnormally huge collagen fibrils and overtly thick basement laminae were revealed by electron microscopy of the lungs from such rats, including those animals exposed

Table 8-4. PATHOLOGICAL CHANGES IN LUNGS OF MICE EXPOSED DAILY TO
940 $\mu\text{g}/\text{m}^3$ (0.5 ppm) NO_2 ON VARIOUS SCHEDULES (40)

Length of total exposure, mo	Daily Exposure, hr		
	6	18	24
3	Pneumonitis characterized by peribronchial and interstitial alveolar lymphocytic infiltration. Bronchiolar epithelium was cuboidal and appeared normal. Some alveolar expansion but no bronchiolar obstruction. Alveolar septal breaks apparent.	Bronchiolar epithelium was cuboidal and appeared normal. Some alveolar expansion, but no bronchiolar obstruction. Alveolar septal breaks apparent.	Obstruction of some respiratory bronchioles with acidophilic substance. In these areas bronchiolar epithelium was columnar and devoid of cilia. Alveoli distal to the obstructed areas were expanded with concomitant thinning of walls. Alveolar septal breaks apparent.
6	Pneumonitis as in 3-month exposure. Bronchial mucosa markedly inflamed with surface erosion and loss of cilia. Bronchiole-alveolar junction partially to totally blocked, with cellular debris in some areas. Bronchiolar epithelium cuboidal. Alveolar expansion and septal breakage as in 3-month exposure.	Pneumonitis. Bronchial mucosal and bronchiole-alveolar junction reactions similar to 6-hour exposure. Bronchiolar epithelium cuboidal. Alveolar expansion and septal breakage as in 3-month exposure.	Pneumonitis similar to that of 6- and 18-hour exposure, but more severe. In some areas and coated with mucoid-like material. Alveolar expansion and septal breaks apparent.
9	Pneumonitis, less severe than shorter-term exposures. Alveolar septal walls thicker. Alveolar expansion not as severe as in 3- and 6-month exposures.	Pneumonitis, less severe than in shorter-term exposures. Alveolar septal walls thicker. Alveolar expansion not as severe as in 3- and 6-month exposure.	Pneumonitis, less severe than in shorter-term exposures. Alveolar expansion not as severe as in 3- and 6-month exposures.
12	Moderate pneumonitis. Evidence of bronchiolar epithelial erosion.	Severe pneumonitis characterized by widespread interstitial and peribronchial lymphocytic infiltration. Evidence of bronchiolar epithelial erosion.	Severe pneumonitis as in 18-hour exposure. Some lung lobes in state of gray hepatization of pneumonia with exudate in alveoli and infiltration of polymorphonuclear leucocytes. Evidences of bronchiolar epithelial erosion.

Table 8-5. PATHOLOGICAL CHANGES IN LUNGS OF RATS CONTINUOUSLY EXPOSED TO NO₂ (41, 42)

Concentration		Length of exposure	Lung weight changes	Histology
ppm	mg/m ³			
25	47.0	37 to 41 days	No difference from control	At 41 days: moderate hypertrophy and hyperplasia of bronchiolar epithelium; columnar type cells, tall; increased numbers of active goblet cells in the major bronchi.
		146 to 157 days	Over double weight of control	At 157 days: advanced hyperplasia and hypertrophy of epithelial cells. Proliferation of connective tissue stroma, some free macrophages and desquamated cells in alveolar spaces. Considerable distension of alveolar ducts and alveoli, septal breaks; change considered emphysematous.
12.5	23.8	About 30 weeks	Increased up to double the weight of controls	Similar to effects at 47 mg/m ³ (25 ppm). In rats surviving long periods of exposure, one had focal nodular metaplasia in bronchial epithelium; two had focal adenomatosis in lung periphery.
4.0	7.5	16 weeks (Experiment stopped)	No difference from controls	Mild hyperplasia of bronchial epithelium in all lungs. Strands of mucous material in bronchial lumen in 2 of 9 animals. Alveolar ducts and some alveoli contained bits of proteinaceous material and scattered macrophages. Otherwise no difference from controls.
2	3.8	Natural lifetime	Increased to about 110% of control	Grossly like controls. Microscopically, bronchiolar epithelial cells were more uniform with few remaining cilia and increased size (area one-third greater than controls). Cells suggested dormancy, lacking most exfoliative activity and cytoplasmic blebbing. Rod-like cytoplasmic inclusion bodies seen.
0.8	1.5	Natural lifetime	No difference from control	Microscopically, essentially unchanged except for occasional evidence of bronchiolar epithelial changes similar to those obtained with 3.8 mg/m ³ (2 ppm).

to as little as 3.8 mg/m^3 (2 ppm) NO_2 (47). Freeman et al. (48) have applied morphometry to the problem of determining whether the enlargement of the lung from NO_2 exposure results from simple hyperinflation or from destruction of inter-alveolar septae. These results convincingly demonstrate that after continued exposure to 28.2 mg/m^3 (15 ppm) NO_2 the total number of air spaces in the entire lung are reduced as much as 50 percent, compared with controls, and that the reduction in alveolar surface area is approximately 25 percent. Functional residual capacities of the lung were also increased over those of controls.

By means of electron microscopy, an ultrastructure study concerned with changes in collagen was conducted on rats. One group was exposed to 37.6 mg/m^3 (20 ppm) NO_2 for 90 days, with recovery periods between exposures, and the other group was exposed to 32.0 mg/m^3 (17 ppm) NO_2 intermittently, also with recovery periods. Recovery intervals were necessary to ensure longevity of animals undergoing lifetime exposure. In rats intermittently exposed, thickening of the basement membranes occurred after 2 to 3 months, together with swelling of the individual fibrils in the connective tissue fibers. These changes became more severe with time, and were quite striking at the termination of the experiment 610 days after beginning of exposure (49).

Early, emphysema-like lesions were also produced in larger animals by exposure to NO_2 . Twelve pure-bred beagle dogs, divided into two equal groups, were exposed continuously for 6 months to either filtered air, or filtered air plus approximately 47.0 mg/m^3 (25 ppm) NO_2 . Autopsies on the NO_2 -exposed dogs revealed bullous emphysema in the lungs of one animal and increased firmness with scattered, small bullae in each of

the remaining five animals. A diffuse increase in collagen was noted in the lungs of all six animals, but no such changes were observed in the controls (50). Further studies suggested that the addition of $1 \mu\text{g}/\text{m}^3$ ferric oxide dust to air containing $48.9 \text{ mg}/\text{m}^3$ (26 ppm) NO_2 may protect dogs against the development of pathological changes; this proved to be the case in a subsequent 6-month experiment (51).

5) Effects of NO_2 Combined With Other Pollutants. Exposure either for 2 hours to $28.2 \text{ mg}/\text{m}^3$ (15 ppm) NO_2 or for 1 hour to 3 percent (v/v) tobacco smoke had only a slight effect on the surface structure of hamster lungs. When hamsters were exposed to the same concentrations for the same times, but sequentially (NO_2 followed by tobacco smoke), the combination of exposures produced marked alterations in surface morphology. The structure of mucus-secreting cells was not typical, and a marked loss of cilia was noted 2 days after exposure. These changes were not reversible. Seven days after exposure, the surface structure of the main bronchi and secondary airways appeared to be even more disrupted; small patches of cilia and deep holes appeared in the bronchial mucosa. The investigators concluded that NO_2 and tobacco smoke act synergistically on the bronchial epithelium, producing pathological changes much greater than those caused by either pollutant alone (52).

Boren (53) exposed guinea pigs to carbon particles and NO_2 . Markedly different results were obtained depending on the sequence of exposure. Inhalation of carbon followed by exposure to NO_2 resulted in lung destruction. When NO_2 was inhaled first and followed with exposure to carbon particles, no destruction of lung tissue was found. This points out the need to consider the sequence of exposure to multiple pollutants in interpreting results.

c. Systemic Effects

1) Tissue Changes. Kidney, liver, and heart tissues of squirrel monkeys exposed to NO_2 for 2 hours were damaged in proportion to the dosage. At 28.2 mg/m^3 (15 ppm), some tubular erosion appeared in the kidneys; liver cells ballooned and developed clear cytoplasm with displaced nuclei and congested interstitial spaces. At 65.8 mg/m^3 (35 ppm), renal glomerular tufts were swollen and heart tissue showed areas of interstitial fibrosis. At 94 mg/m^3 (50 ppm), the hearts developed interstitial edema and kidney and liver tissue were infiltrated by lymphocytes. Centrolobular necrosis also appeared in the liver (17).

Tissue cultures of lung, cardiac muscle, liver, skin, and frontale of chicken embryos were exposed to 0.9 to 28 mg/m^3 (0.5 to 15 ppm) NO_2 for 5 hours. All tissues clearly showed inhibition of cell growth within the next 24 hours. Seven days after the exposure, some tissues had recovered completely (liver), whereas others (skin) reacted by regenerating, through stimulation of secondary cell growth from within the explantate, all the peripheral cells lost. The lowest concentration of NO_2 at which effects were observed was 1.9 mg/m^3 (1 ppm). No increased effects were noted at concentrations beyond 9 mg/m^3 (5 ppm). The highest concentration tested was 28 mg/m^3 (15 ppm) (54).

2) Weight Loss. Studies on the effects of long-term exposure to NO_2 have produced conflicting results with respect to weight loss. No significant reduction in the rate of weight gain was noticed in rabbits, guinea pigs, rats, or hamsters exposed to 1.9, 9.4, or 47 mg/m^3 (1, 5, or 25 ppm) NO_2 or in dogs exposed to 1.9 and 9.4 mg/m^3 (1 and 5 ppm) NO_2 for 6 hours a day for 18 months (19). Furthermore, no significant differences in weight gains appeared in mice exposed to $940 \text{ } \mu\text{g/m}^3$ (0.5

ppm) NO_2 for 6, 18, or 24 hours a day, 5 days a week, for up to 12 months (47,55). Combined NO_x exposures of 940 to 1880 $\mu\text{g}/\text{m}^3$ (0.5 to 1.0 ppm) NO_2 plus 245 $\mu\text{g}/\text{m}^3$ (0.2 ppm) NO or of 2.8 to 3.8 mg/m^3 (1.5 to 2.0 ppm) NO_2 plus 245 $\mu\text{g}/\text{m}^3$ (0.2 ppm) NO 16 hours a day for 18 months did not change weight gain in the 12 beagles in either experiment.

In contrast, rats exposed continuously to 22.6 mg/m^3 (12 ppm) NO_2 for 9 months continued to grow, but their body weights remained 20 percent below those of control animals (39,42). One observer (56) reported a 10 percent weight loss in rabbits exposed to 5.6 mg/m^3 (3 ppm) NO_2 for 15 weeks, while controls added 11 percent to their weight. The effect was apparently dose dependent, for rabbits exposed to 2.5 mg/m^3 (1.3 ppm) NO_2 for 17 weeks showed a weight increase of 2 percent while controls showed an increase of 8 percent. In rats exposed to concentrations of 4.7 to 6.6 mg/m^3 (2.5 to 3.5 ppm) NO_2 for 3 months, the weight of the spleen increased. This effect disappeared upon continued exposure (57).

While no quantitative changes were described, the gain in weight of the spleen might reflect hyperplasia of erythrogenic components, a view that is congruent with the transient polycythemia reported below for NO_2 exposures.

3) Physical exertion: During six-hour exposures of 6.9 to 39.3 mg/m^3 (3.7 to 20.9 ppm) NO_2 , the voluntary running activity of male mice was depressed when the concentration was 14.5 mg/m^3 (7.7 ppm) or greater. Although the threshold was not identified, it could be narrowed to between 6.9 and 14.5 mg/m^3 . In all cases, activity returned to normal on the first post-exposure day (4).

The influence of NO_2 on performance of rats during physical exertion was measured by means of a modified swimming test, employing a

4 m swimming distance (58). The test was repeated 20 times per trial for a total of 80 m, with a 20 second rest after each 4 m distance. The rats had to perform the test while exposed to 37.6 mg/m^3 (20 ppm) NO_2 ; the total exposure time was approximately 15 min. The test was repeated 3 times a week. Exposed animals showed a marked decrease in swimming speed from the second month of the experiment, while controls improved in performance as a result of training. In rats exposed to 9.4 mg/m^3 (5 ppm) NO_2 , a decrease of 25 percent in performance occurred in the 5th and 6th weeks of the experiment. During the whole course of the experiment the controls performed better than the exposed animals ($p=0.01$). Even animals exposed to 1.9 mg/m^3 (1 ppm) NO_2 showed a slight tendency toward decreased performance. The difference, however, was not significant (59).

Figure 8-3 shows the development in physical performance of rats over 6 weeks. The time the animals needed to swim a certain distance at the beginning of the experiment was set as 100 percent. A 25 percent increase in time signifies a 25 percent decrease in performance. The different performance of the controls is attributed to an age difference between the groups.

4) Hematologic Effects. Exposure to nitrogen dioxide alters the circulating cellular constituents. Studies of the effects of NO_2 on the circulating blood have included both short- and long-term exposures. In one short-term study, researchers (60) exposed dogs to 73.3 and 99.6 mg/m^3 (39 and 53 ppm) for 60 minutes, to 97.8 and 160 mg/m^3 (52 and 85 ppm) for 15 minutes, and to 235 and 308 mg/m^3 (125 and 164 ppm) for 5 minutes; they found no changes in hematocrits and blood platelet counts determined 4, 24, 48, and 72 hours after exposure. The same was true in dogs exposed to 1.9 and 47.0 mg/m^3 (1 and 25 ppm) NO_2 6 hours a day for

18 months (19).

Freeman et al. (45) found polycythemia in rats allowed to breathe 3.8 mg/m^3 (2 ppm) NO_2 or more, continuously. The concentration of erythrocytes rose within 2 to 3 weeks and achieved levels of about 40 to 100 percent above baseline values. After some delay, both hematocrit and hemoglobin levels rose, but to a lesser degree, so that the fully

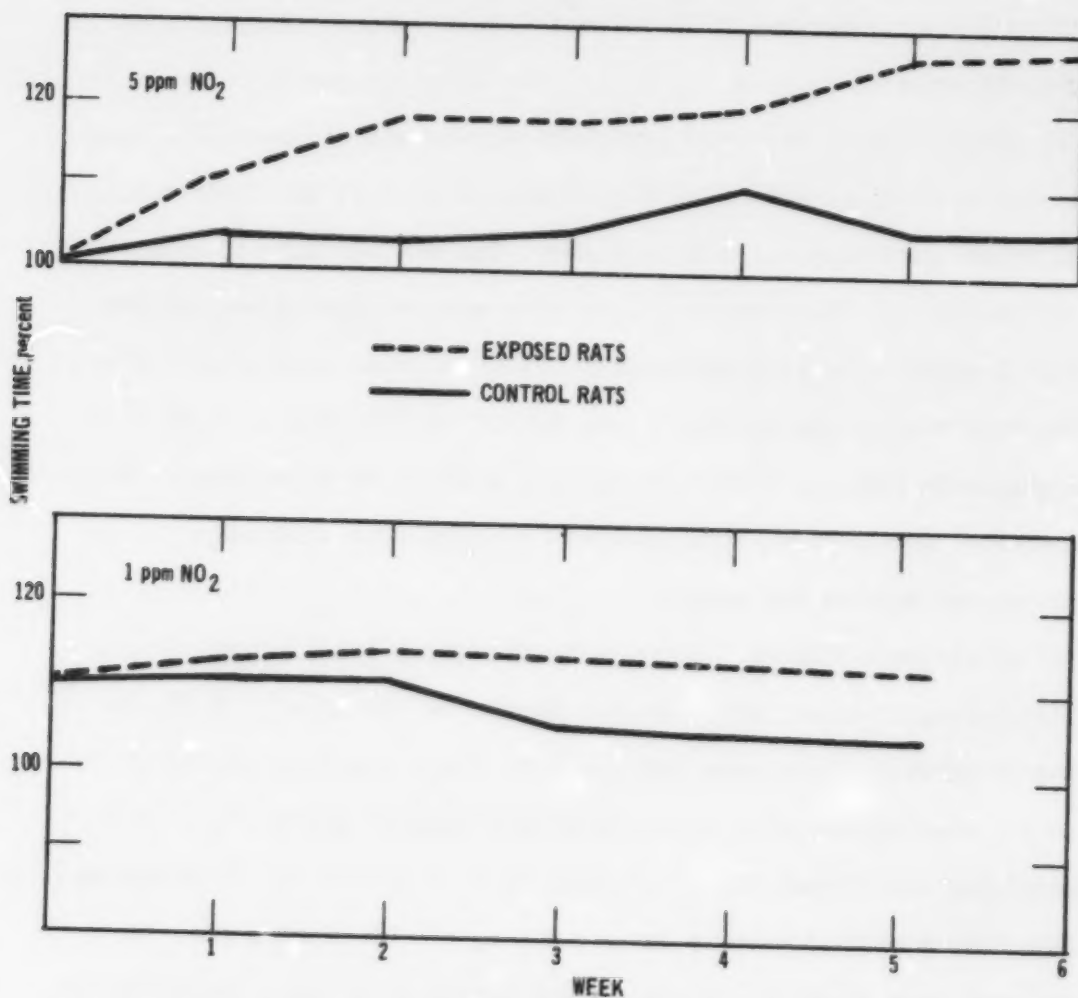


Figure 8-3. Influence of NO_2 on time needed to swim a specific distance.

developed polycythemia was characterized by a reduction in mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. Cellular diameters measured on the flat surface of stained smears were normal. The blood of monkeys (M. speciosa) exposed to 3.8 and 16.9 mg/m³ (2 and 9 ppm) NO₂ followed a similar course (45). The polycythemia was transient in rats, with effects declining after exposure of approximately 3 months' continuous exposure. When the concentration of the NO₂ was raised, however, polycythemia again developed.

Leukocytosis occurred in the peripheral blood of rabbits exposed to both 2.5 and 5.6 mg/m³ (1.3 and 3.0 ppm) NO₂ for 15 to 17 weeks but it receded with cessation of exposure. The leukocytic response was accelerated by the presence of SO₂. Phagocytic activity was depressed by NO₂ and both leukocytic and phagocytic alterations were greater at the higher NO₂ exposure (56). The chemical action of NO₂ on the erythrocyte is at this time poorly understood. While methemoglobin (MeHb) and NO₂-hemoglobin are readily formed from in vitro exposure of blood cells, no great effect from in vivo exposure is consistently reported. This appears paradoxical in the face of reports by Svorcova (61) that NO₂ is rapidly converted to nitrite (NO₂⁻) and nitrate (NO₃⁻) in the lungs and that these ions appear immediately in the blood and, shortly after, are excreted in the urine. Fifteen minutes after the beginning of exposure to 45 mg/m³ (24 ppm) NO₂ both nitrite and nitrate could be detected in the urine of rabbits. It would appear reasonable to speculate that methemoglobinemia does occur from NO₂

exposure but that at concentrations approaching ambient levels there is insufficient increase over background to be detectable. According to Wagner (9), no detectable elevation of MeHb was evident in rats exposed to 9.4 mg/m^3 (5 ppm) for as long as 10 months, whereas 1 hour's exposure to 18.8 mg/m^3 (10 ppm) caused approximate doubling of the background level. Reports from previous investigators who have studied the problem are reviewed below. Cats, rabbits, guinea pigs, mice, and rats were exposed to 56.4 to 1880 mg/m^3 (30 to 1000 ppm) NO_2 for unspecified periods of time. Methemoglobin was not detected in animals receiving up to 103 mg/m^3 (55 ppm) NO_2 . Cats exposed to 188 mg/m^3 (100 ppm) showed detectable amounts of MeHb after approximately 1 hour of exposure, however. At concentrations of 282 mg/m^3 (150 ppm) NO_2 and above, the blood of all animals tested contained MeHb after 1 hour of exposure, but the MeHb was no longer measurable 1 to 2 hours after animals were returned to clean air. In these experiments, the NO_2 values reflected the total oxides of nitrogen present in the exposure chamber; the concentration of NO was not evaluated separately (62).

In other experiments, MeHb appeared in the blood of rabbits and rats exposed to fumes produced in the electric-arc welding process (63). Rats exposed for 6 hours a day, 5 days a week, for 43 days, to fumes containing 45.1 mg/m^3 (24 ppm) NO_2 developed 4.5 to 21.7 percent MeHb (mean of 13.6 percent). Detectable levels were still present on the 11th day of the post-exposure period. Rabbits similarly exposed for 45 days formed an average of 2.8 percent MeHb (range 0.9 to 4.5 percent). On the 6th day of the post-exposure period, detectable amounts remained in male rabbits only. Male rats exposed to 132 mg/m^3

(70 ppm) NO_2 for 6 hours a day formed 2.6 percent MeHb after the 1st day of exposure and 3 percent by the 3rd day. Three days after exposure, the levels were within the control range. In these experiments, it was estimated that between 12 and 17 percent of the nitrous fumes existed as NO (63).

A mixture of 180 ppm NO_2 plus N_2O_4 caused death in 12 dogs within 55 to 285 minutes. Methemoglobin concentrations increased significantly ($p < 0.01$), with an average of 325 mg per 100 g of blood before, and 700 mg per 100 g after, exposure (64).

5) Immunologic Effects. A circulating substance with properties similar to a lung antibody appeared in the serum of guinea pigs exposed to 9.4 mg/m^3 (5 ppm) NO_2 either 4 hours a day, 5 days a week, or 7.5 hours a day, 5 days a week, for up to 5.5 months. In a second group, exposed to 28.2 mg/m^3 (15 ppm) NO_2 continuously for 1 year, the antibody reacted in vitro with proteins extracted from the lung tissue of control animals. The titers of reactive substances increased with the intensity and duration of exposure, but no absolute values were ascribed to the data because the latex agglutination method employed is not quantitative (18).

6) Effects on Enzyme Systems. The effects of exposure to 28.2 mg/m^3 (15 ppm) NO_2 continuously for 10 weeks on oxygen consumption, lactic dehydrogenase, and aldolase in guinea pig lung, liver, spleen, and serum were determined (65). The following significant changes occurred: oxygen consumption increased in spleen and kidney; lactic dehydrogenase activity increased in lung, liver, and kidney; and aldolase activity increased in tissues. Short-term exposures also caused a significant increase in the activities of the same enzymes in some tissues. Exposure of guinea pigs to 75.2 mg/m^3 (40 ppm) for 30 minutes at 2-hour intervals

for a total of 4.5 hours produced the following significant changes: oxygen consumption increased in liver, spleen, and kidney; lactic dehydrogenase activity increased in liver, kidney, and serum; and aldolase activity increased in liver, spleen, kidney, and serum. The mechanism that causes these enzymatic changes is not known, but it might reflect a general response to stress.

Following a 2-hour exposure to 65.8 and 94.0 mg/m³ (35 and 50 ppm) NO₂, lactic dehydrogenase isoenzymes from lung tissue of squirrel monkeys shifted to predominantly anaerobic band 5 when chromatographed, and after a 2-hour exposure to 18.8 mg/m³ (10 ppm) NO₂, a similar increase in band 5 was noted in serum lactic dehydrogenase isoenzymes. This change in isoenzyme pattern was present at 2 days, but returned to normal 8 days after termination of the NO₂ exposure. A similar shift to anaerobic isoenzyme was observed in the heart tissue of hamsters exposed for 2 hours to 9.4 and 65.8 mg/m³ (5 and 35 ppm) NO₂ (17, 66).

d. Susceptibility to Respiratory Infection

1) Bacteria and Influenza. A study of rabbits exposed to concentrations of NO₂ ranging from ambient Cincinnati levels to 113 mg/m³ (60 ppm) revealed increased numbers of polymorphonuclear leukocytes (heterophiles) in lung washings; this condition persisted for more than 72 hours after a single 3-hour exposure. When streptococci were instilled into lungs of NO₂-exposed, anesthetized rabbits 30 minutes before lavage, a pronounced inhibition of phagocytic activity was observed in comparison to controls (67).

Exposure of mice, hamsters, and squirrel monkeys to NO₂ increased susceptibility to bacterial pneumonia and influenza infection. This

susceptibility, observed in both short- and long-term exposures, is based on three parameters: 1. increased mortality rates; 2. reduced survival times; and 3. reduced ability to clear inhaled infectious agents from the lungs, as determined by the number of viable organisms that can be cultured from the lungs. Mice in these experiments were exposed for 2 hours to NO₂ in concentrations ranging from 2.8 to 47.0 mg/m³ (1.5 to 25 ppm), and then challenged with an aerosol of Klebsiella pneumoniae within 1, 6, and 27 hours after the NO₂ exposure (68,69). The minimum NO₂ concentrations required to produce a statistically significant rise in subsequent mortality was 6.6 mg/m³ (3.5 ppm) for 2 hours when the infectious challenge took place 1 hour after the NO₂ exposure. When the infectious challenge was delayed, a statistically significant effect was noted at 6, but not at 27 hours, at NO₂ concentrations of 9.4 mg/m³ (5 ppm) and above. Exposure to 47.0 mg/m³ (25 ppm) NO₂ 6 and 14 days prior to the challenge with K. pneumoniae did not increase mortality. The same authors reported that when mice were infected with K. pneumoniae first, and then exposed for 2 hours to 47.0 mg/m³ (25 ppm) NO₂ within 1, 6, 27, 48, and 72 hours after the infectious challenge, the mortality increase was statistically significant. This effect was not observed at 4.7 mg/m³ (2.5 ppm) NO₂.

A 2-hour exposure to 9.4 mg/m³ (5 ppm) NO₂ in various inbred strains of mice (BDF₁, BALB/c, C57BL, and LAF₁), either before or after infectious challenge with an aerosol of K. pneumoniae, favored increased mortalities. A similar enhancement in mortality was observed in hamsters exposed for

2 hours to 65.8 mg/m^3 (35 ppm) NO_2 and above, and challenged with K. pneumoniae (66).

The rate of clearance of inhaled bacteria from the lungs of mice and hamsters was reduced upon short-term exposure to NO_2 (66). The animals were exposed to 9.4 mg/m^3 (5 ppm) NO_2 for 2 hours, and within 1 hour challenged with K. pneumoniae aerosols. Immediately, and at 1, 3, 5, 6, 7, and 8 hours after the infectious challenge, the animals were sacrificed and K. pneumoniae in lungs was quantitatively assayed. In control animals, the bacterial population was markedly reduced during the 6 hours following the challenge. Thereafter, the population increased, reaching its initial concentration after approximately 8 hours. In mice and hamsters exposed to 9.4 mg/m^3 (5 ppm) NO_2 , the period of initial clearance was reduced to 4.5 and 5 hours, respectively, and the original concentration was reestablished in less than 7 hours (64).

In a long-term study, Ehrlich and Henry (55,70) exposed four groups of mice to $940 \text{ } \mu\text{g/m}^3$ (0.5 ppm) NO_2 for 6, 18, and 24 hours a day, 7 days a week, for up to 12 months. The mice were challenged with an aerosol of K. pneumoniae after 1, 3, 6, 9, and 12 months of exposure. Statistically significant increases in mortality were observed after continuous exposure to $940 \text{ } \mu\text{g/m}^3$ (0.5 ppm) for 3 months, and after 6- and 18-hour-a-day exposures for 6 months. After 12 months of exposure, mortality rates increased significantly **only** when the NO_2 exposure was continuous. The clearance rate of viable bacteria from the lungs of mice was also affected by long-term exposure to $940 \text{ } \mu\text{g/m}^3$ (0.5 ppm) NO_2 . In mice exposed to NO_2 for 6 and 18 hours a day

for 9 months, some reduced capacity to clear bacteria from lungs was observed, and after 12 months of exposure a significant inhibition of bacterial clearance was apparent. Mice exposed to NO_2 for 24 hours a day showed a significantly reduced capacity to clear viable bacteria after 6, 9, and 12 months of exposure.

Henry et al. (17) exposed squirrel monkeys to 18.8 to 94.0 mg/m^3 (10 to 50 ppm) NO_2 for 2 hours and challenged them by the intratracheal route with K. pneumoniae. Exposure to 94.0 mg/m^3 (50 ppm) NO_2 for 2 hours was not fatal, whereas the same exposure followed by challenge with K. pneumoniae was fatal to three out of three monkeys. Squirrel monkeys exposed to 18.8 mg/m^3 (10 ppm) NO_2 for 2 hours and then challenged with K. pneumoniae had bacteria present in their lungs 19 to 51 days after challenge. In many bronchioles, epithelial cilia were missing, cells had proliferated, and lymphocytes and polymorphonuclear cells had infiltrated the collapsed areas.

The same group (71) exposed male squirrel monkeys continuously to NO_2 and challenged them with K. pneumoniae aerosols. Out of four monkeys exposed to 18.8 mg/m^3 (10 ppm) NO_2 for 1 month, one died and two had the infectious agent present in the lungs at autopsy. Two out of seven monkeys exposed to 9.4 mg/m^3 (5 ppm) NO_2 for 2 months died, and five had the infectious agent present in the lungs at autopsy.

Squirrel monkeys were also experimentally infected with influenza A/PR-8 virus 24 hours before continuous exposure to 18.8 and 9.4 mg/m^3 (10 and 5 ppm) NO_2 . All six monkeys exposed to 18.8 mg/m^3 (10 ppm) died within 3 days, and one out of three exposed to 9.4 mg/m^3 (5 ppm) succumbed to the disease. There were no deaths in the control group challenged with influenza virus (69).

When the squirrel monkeys were exposed to 9.4 mg/m^3 (5 ppm) NO_2 for 5 months and, during the exposure, challenged three times intratracheally with the influenza A/PR-8 virus, the formation of protective serum neutralization antibody appeared to be depressed as evidenced by serum neutralization antibody titers and hemagglutination-inhibition titers (72).

2) Bacteria and Tobacco Smoke. Combined exposures to NO_2 , tobacco smoke, and K. pneumoniae were reported for hamsters (52, 73). A 2-hour exposure to 28.2 mg/m^3 (15 ppm) NO_2 followed by 1-hour exposure to 3 percent (v/v) tobacco smoke significantly decreased the resistance to bacterial pneumonia, as evidenced by increased mortalities. Furthermore, exposure to NO_2 plus tobacco smoke reduced the rate of clearance of viable bacteria from the lungs of hamsters to a greater extent than exposures to the individual pollutants. The combined exposure produced irreversible, marked alterations in surface morphology of lung tissue. The typical structure of mucus-secreting cells was not present, and a marked loss of cilia was noted 2 days after exposure.

3) Interferon Formation. Impairment of interferon (an antiviral substance), formation by NO_2 exposure has been demonstrated by challenging rabbit alveolar monocytes with parainfluenza-3 virus (74). Rabbits exposed to 49.0 mg/m^3 (25 ppm) NO_2 for 3 hours, either immediately after, or at 0, 3, 6, 12, or 24 hours before inoculation with rabbit pox virus, failed to develop the anticipated resistance to infection. This inhibition of resistance persisted for at least 96 hours after the NO_2 exposures. During this period, alveolar monocytes from NO_2 -exposed animals were unable to produce interferon in vitro when inoculated with the parainfluenza-3 virus.

2. Effects in Man

a. Experimental Exposures

1) Odor Perception. In a series of experiments with healthy male volunteers between the ages of 20 and 35 years, individuals were exposed to varying concentrations of NO_2 in a specially designed chamber, and the olfactory threshold was measured under various conditions (Table 8-6). At a concentration of $225 \mu\text{g}/\text{m}^3$ (0.12 ppm) NO_2 , only a few subjects perceived the odor immediately. Perception was immediate in over half of the subjects exposed to $415 \mu\text{g}/\text{m}^3$ (0.22 ppm) NO_2 . At higher concentrations, beginning at $835 \mu\text{g}/\text{m}^3$ (0.42 ppm) NO_2 , all subjects recognized the odor immediately. Persistent recognition of the odor varied considerably, ranging from a few minutes at the lower exposure levels to over 30 minutes at some of the higher concentrations (75).

In another study (76) of 14 subjects, the NO_2 olfactory threshold was $225 \mu\text{g}/\text{m}^3$ (0.12 ppm). The effect of NO_2 and SO_3 was additive, i.e., a lower concentration of each gas led to odor perception if both gases were present simultaneously.

In a study of diesel exhaust odor in 1969, it was found that NO_2 may contribute to the odor of diesel exhaust. An assessment of the major industrial odorants in diesel exhaust revealed that the mixture with the greatest odor contained about $940 \mu\text{g}/\text{m}^3$ (0.5 ppm) NO_2 (77).

2) Pulmonary Function. In one study of pulmonary function, exposure to NO_2 was controlled in a special room equipped with an air filter (78). Six normal subjects and four patients with "moderate to marked" pulmonary disease were exposed to concentrations of 940 to $5640 \mu\text{g}/\text{m}^3$ (0.5 to 3 ppm) NO_2 on several occasions for 2 to 3 hours at a time.

Table 8-6. RECOGNITION OF NO₂ ODOR BY HEALTHY YOUNG ADULT MEN AFTER
VARIED EXPOSURES IN AN EXPERIMENTAL CHAMBER (75)

Concentration ^a		Odor perception on entry to chamber		
mg/m ³	ppm	Subjects	Number of subjects	Duration ^a min
0.225	0.12 (0.1-0.15)	9	3	5 (0.5-10)
0.415	0.22 (0.16-0.28)	13	8	3 (1-10)
0.835	0.42 (0.39-0.46)	5	8	2.5 (1-5)
8.0	4.0 (3.0-4.2)	12	12	5.5 (3-10)
19.9	10.6 (10.1-11.2)	4	4	8 (6-13)
39.9	19.7 (19.3-20.1)	8	8	12 (5-24)
56.8	30.2 (29.1-31.4)	3	3	32 (25-40)

^aThe range of actual measured values is included in parentheses.

Physiological parameters were measured before, during, and after exposure, with subjects at rest or exercising. Smokers were not excluded from the study, but were required to abstain from smoking for the 8-hour period prior to the chamber study. The data showed no consistent changes in airway resistance, pulse rate, respiratory rate, or subjective complaints that could be related to the NO₂ challenge.

Nitrogen dioxide and SO₂ produced additive effects on pulmonary function in five healthy males, ages 21 to 40, who were judged to be

free from respiratory disease (79). One subject smoked 5 to 6 cigarettes a day. Each subject was exposed on separate occasions to 7.5 to 9.4 mg/m³ (4 to 5 ppm) NO₂ and 10.5 to 13.1 mg/m³ (4 to 5 ppm) SO₂. Each exposure was for 10 minutes, at 2-week intervals. The subjects wore nose clips and inhaled the gas-air mixtures through a mouthpiece. Inspiratory and expiratory flow resistance and pulmonary compliance were measured before, immediately after, and 10, 20, and 30 minutes after exposure. Vital capacity, FEV₁ (1-second forced expiratory volume), maximal mid-expiratory flow rate, and peak flow rate were measured prior to and 30 minutes after exposure. Inhalation of NO₂ caused an increase in both inspiratory and expiratory flow resistance, the maximum recorded increase occurring 30 minutes after the end of exposure. No data were given for the recovery time. Mean pulmonary compliance was unchanged immediately after exposure, but was slightly decreased 30 minutes after exposure (significant at p < 0.10 but not at < 0.05). Lung volumes and peak flow rates did not change significantly. Inhalation of SO₂ caused an increase in both inspiratory and expiratory flow resistance that was maximal immediately after inhalation but was restored to pre-exposure levels 30 minutes later.

Exposure to a mixture of 4.7 mg/m³ (2.5 ppm) NO₂ and 6.6 mg/m³ (2.5 ppm) SO₂ produced a bimodal increase in both inspiratory and expiratory flow resistance. The first increase, which corresponded to the effect of SO₂ alone, occurred immediately after exposure. The second increase in resistance corresponded to the effect of NO₂ alone, and was maximal 30 minutes after exposure. Sulfur dioxide is known to cause an immediate, reflexive increase in airway resistance along

parasympathetic pathways (80). The mechanism by which NO_2 induces resistance is unknown, but the delay suggests that the mechanism differs from that of SO_2 (79).

Recent experimental studies by von Nieding et al. have clearly demonstrated the effect of NO_2 exposure on pulmonary ventilation in human volunteers. After short exposures (15 minutes) to low concentrations (9.4 mg/m^3 or 5 ppm) of NO_2 , a decrease of alveolar ventilation and an inequality of distribution of alveolar ventilation was observed among healthy volunteers and chronic bronchitics. The method used for assessment was registration of the washout of argon, an inert gas. After healthy individuals inhaled 9.4 mg/m^3 (5 ppm) NO_2 for 15 minutes, the number of breaths needed to eliminate 99 percent of the initial concentration of the test gas after rebreathing room air increased from 25 to 35 for the second compartment. This happened in spite of a slight increase in respiratory rate. Among chronic bronchitis patients, the average number of breaths increased from about 28 to 50 and more (21,81).

Respiratory gas exchange was studied in one group each of healthy subjects and chronic bronchitics after short-term exposure to NO_2 . In both groups, arterial oxygen partial pressure (PaO_2) decreased when 9.4 mg/m^3 (5 ppm) NO_2 was inhaled for 15 minutes. The average reduction was about 7 torr for both groups ($p < 0.001$ and $= 0.02$). The end-expiratory oxygen partial pressure (PAO_2) remained practically unchanged ($p > 0.1$). The end-expiratory-arterial oxygen partial pressure difference (A-aDO_2) showed a corresponding increase ($p < 0.001$) (Figure 8-4). At 7.5 mg/m^3 (4 ppm) the effect was still significant, whereas no effect was observed at 3.8 mg/m^3 (2 ppm) (81,82). Pro-

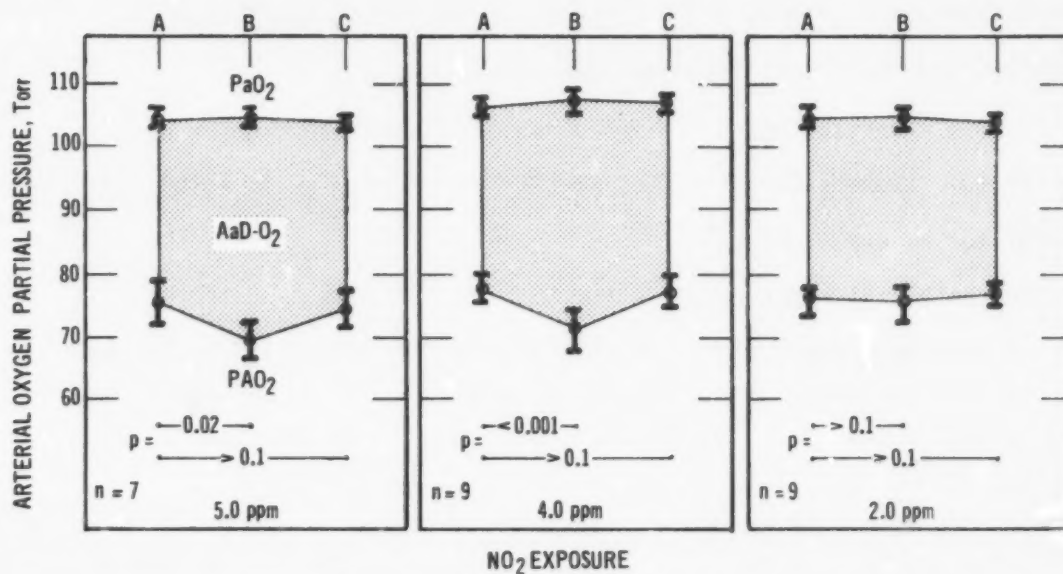


Figure 8-4. Influence of NO_2 on arterial oxygen partial pressure in human subjects; mean values and standard deviations for PaO₂ and PAO₂ before (A), at the end of 15-minute exposure (B), and 15 minutes after cessation of the NO_2 inhalation (C).

longation of the exposure at the 9.4 mg/m^3 (5 ppm) level produced no increment in the effect (21). Nitrogen dioxide concentrations of 9.4 mg/m^3 (5 ppm) caused a slight but significant increase of the pressure in the arteria pulmonalis in 10 healthy subjects. The average pressure increase after a 15-minute exposure to 9.4 mg/m^3 (5 ppm) was 1.6 mm Hg ($p < 0.001$) (81).

A highly sensitive indicator of an effect of NO_2 on the respiratory tract seems to be changes in airway resistance (R_t). Below a concentration of 2.8 mg/m^3 (1.5 ppm), no significant difference could be found. Inhalation of NO_2 concentrations of 3.0 to 3.8 mg/m^3 (1.6 and 2.0) produced a slight but significant increase in airway resistance.

At concentrations above 3.8 mg/m^3 (2.0 ppm), the increase became more pronounced (Figure 8-5). This effect on airway resistance was blocked by an antihistamine (Mecloastine) (82,83).

No differences between effects on smokers and non-smokers was observed. Smokers were told to refrain from smoking at least 2 hours prior to the experiment.

b. Occupational Exposures.

There are numerous possibilities for occupational exposure to NO_x .

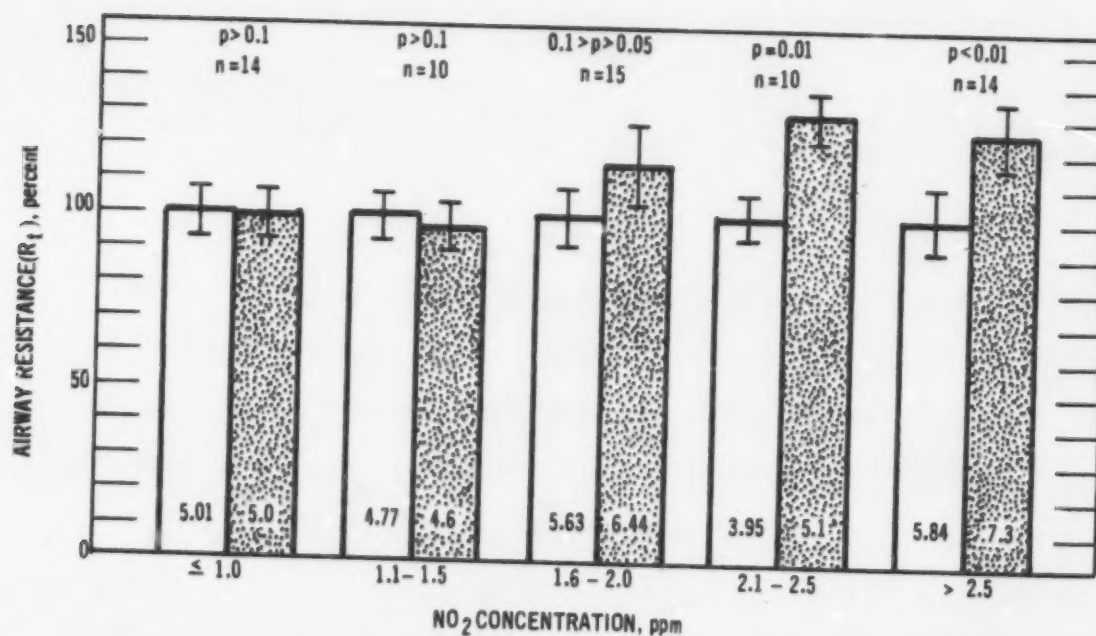


Figure 8-5. Influence of NO_2 on airway resistance before and immediately after inhalation of NO_2 at different concentrations (initial value = 100 percent).

Hazardous occupations include the manufacture of NO, nitration of cellulose, and other organic materials; electric-arc welding; and photoengraving. Accidental exposures have resulted from inhaling gases from the combustion of celluloid and nitrocellulose films, and from inhaling silage gas.

Four clinical types of poisoning resulting from occupational exposures (84) have been encountered: 1. irritant gas poisoning, 2. reversible poisoning, 3. shock, and 4. combinations of the other three. Irritant gas exposure is characterized initially by pain, burning, and choking in the throat and chest; violent cough; and the expectoration of yellow-tinged sputum. Reversible poisoning is characterized by dyspnea, cyanosis, vomiting, vertigo, somnolence, a feeling of intoxication, fainting, loss of consciousness, and methemoglobinemia. Persons suffering this type of poisoning do not develop pulmonary edema, and, if removed from the exposure early enough, may recover completely. Otherwise, the poisoning may rapidly become fatal. Patients whose exposure produces shock immediately show severe symptoms of asphyxiation, convulsions, and respiratory arrest; death is presumably the result of stasis in the pulmonary circulation. This form of NO_x poisoning is exceptional and may result from the sudden inhalation of high concentrations. In the combined type, the patient immediately shows symptoms referable to the central nervous system, such as vertigo, somnolence, and a staggering gait. There may be cyanosis as well. After apparent recovery, this stage may be followed some hours later by progressive dyspnea, marked cyanosis, and pulmonary edema.

Several accidental exposures to silage gas (85,86), which may contain very high concentrations of NO₂, have been reported. In

several instances the exposure proved fatal. One man died 20 hours after being exposed to this type of gas for 5 to 8 minutes (86). One person exposed at the same time for 2 to 3 minutes survived, although he suffered acute pneumonitis. Exposure to NO_2 has been divided into six categories, with corresponding clinical syndromes:

1. Exposure to 940 mg/m^3 (500 ppm) or higher produces acute pulmonary edema and death within 48 hours.
2. Exposure to 564 to 752 mg/m^3 (300 to 400 ppm) produces pulmonary edema with broncho-pneumonia and death in 2 to 10 days.
3. Exposure to 282 to 376 mg/m^3 (150 to 200 ppm) produces bronchiolitis fibrosa obliterans, which is fatal in 3 to 5 weeks.
4. Exposure to 94 to 188 mg/m^3 (50 to 100 ppm) produces bronchiolitis with focal pneumonitis lasting 6 to 8 weeks, followed by spontaneous recovery.
5. Exposure to NO_2 in the range of 47 to 141 mg/m^3 (25 to 75 ppm) produces varying degrees of bronchitis and broncho-pneumonia, but patients recover completely.
6. Chronic intermittent exposure to concentrations of NO_2 on the order of 18.8 to 75.2 mg/m^3 (10 to 40 ppm) may produce chronic pulmonary fibrosis and emphysema.

Occupational exposure to NO_2 is frequently encountered in the use of a variety of welding processes. Evaluation of responses to inhalation of such fumes is complicated by the presence of other contaminants, predominantly NO , ozone, manganese fumes, ferric oxide fumes,

and particulates of various types. In a case of acute poisoning from NO_x from an oxyacetylene torch, a welder died from chemical pneumonitis 10 days later (87). Other workers present during the exposure developed coughs and other respiratory symptoms. Random air samples obtained under simulated conditions revealed NO_x in the range of 71.4 to 662 mg/m^3 (38 to 352 ppm) expressed as NO_2 . After a 3-minute exposure to fumes containing 395 to 714 mg/m^3 (210 to 380 ppm) NO_2 , welders developed a dry cough and tightness in their chests. These symptoms disappeared when they returned to clean air.

Pulmonary edema developed 18 hours after a 30-minute accidental exposure to the fumes of an oxyacetylene torch estimated to have produced approximately 169 mg/m^3 (90 ppm) NO_2 . In pulmonary function tests conducted at that time, vital capacity was only 50 percent of the expected level, but the 0.5-, 1.0-, and 2.0-second FEV's were not diminished (88).

The effects of electric-arc welding exposures from both bare and coated rods have also been examined. In an experiment in which bare rods were used, two men were exposed to the fumes of the electric-arc welding process for 190 minutes (63,89). The average concentration of nitrous fumes, expressed as NO_2 , was 158 mg/m^3 (84 ppm), with an average maximum of 175 mg/m^3 (93 ppm) that lasted for 40 minutes and a peak of 194 mg/m^3 (103 ppm) lasting 5 minutes. These concentrations, measured by the total nitrate method, actually included an unspecified mixture of NO , NO_2 , and N_2O_4 . Subjects were also exposed to approximately 785 $\mu\text{g/m}^3$ (0.4 ppm) ozone throughout the period. They reported no headache, eye irritation, throat irritation, or other ill effects.

In welders exposed to the fumes from electric-arc welding in which coated rods were used (63), for the same length of time, the average MeHb concentration was 2.5 percent and the maximum was 3 percent. The concentration of "nitrous gas" in the working area did not exceed 25 mg/m³ (13.3 ppm), expressed as NO₂, of which not more than 20 percent was estimated to be NO.

The possible long-term effects of occupational exposure to nitrous fumes was reported by Becklake et al. (90) in a study of seven miners who were accidentally exposed to nitrous fumes for periods of 5 to 75 minutes and who developed pulmonary edema 3 to 27 hours after exposure (Table 8-7). The investigators studied pulmonary function at the time of each patient's discharge from the hospital and compared yearly follow-up examination data with corresponding data from 16 normal persons.

Among the seven patients, the most common effects were a reduction in maximal breathing capacity and an increase in expiratory resistance; the latter functional impairment was common to all the patients who complained of exertional dyspnea. In the two patients who felt that their capacity for work was unaffected by the accident, tests showed that pulmonary function had returned to normal during the study period. Chest roentgenograms of those patients with more than 6 years of underground mining service, taken within a year prior to the exposure, had been normal. Following the accident, the arterial oxygen saturation was not affected either at rest or during exercise. The mixing index, a measure of efficiency in clearing nitrogen gas from the lungs, was significantly different from predicted values in four patients, although it returned to normal in the

Table 8-7. RESPIRATORY EFFECTS OF EXPOSURE TO NITROUS FUMES (90)

(Summary of Clinical Data)

Subject age, years	Time after accident, months	Lung volume					FRC/TLC, ^a %	RV/TLC, ^b %	Maximal breathing capacity, c				Non-elastic resistance, cm/liter-sec		Respiratory rate, liters/sec	Dyspnea ^d after accident
		Vital capacity		Residual volume		Mixing index			liters/min	% of expected	Compliance, liters/cm H ₂ O	Inspiration	Expiration			
		liters	% of expected	liters	% of expected											
33	8	2.56	53 ^e	1.93	116	69 ^e	42 ^e	5.66 ^e	71	44 ^e	0.173	1.84	4.04	26	3	
	55	3.48	74 ^e	1.53	81	58	30	3.29	68	43 ^e						
	64	3.98	85 ^e	1.74	92	51	30	3.35	85	54 ^e						
	65							2.74								
35	1	3.8	72 ^e	1.79	87 ^e	47	32 ^e	7.44 ^e	89	53 ^e					0	
	2	4.33	83 ^e	1.77	86 ^e	45	29	3.63 ^e	141	84 ^e						
	6	4.81	92	1.93	94	47	28	2.92 ^e	158	95						
	24	4.80	93	1.55	74 ^e	40	24	2.32	146	90 ^e						
21	37	4.80	93	2.41	114	40	33 ^e	2.45	184	114	0.174	3.65	4.50	12		
	1	5.09	100	1.69	106	61 ^e	25	2.34	139	81 ^e						
	32	5.66	114	1.46	88	59	20	1.90	186	113						
	20	3	3.81	77 ^e	2.28	154 ^e	52	36 ^e	2.03	75						42 ^e
31	15	4.59	94	1.86	124 ^e	49	28	1.95	137	78 ^e	0.249	6.76	5.89	22	2	
	26	4.48	92	1.41	107	63 ^e	24	1.51	149	87 ^e						
	1	5.52	102	2.02	100	54	27	3.59 ^e	130	75 ^e						
	4	5.51	102	1.80	89	57	24	2.46	152	87 ^e						
49	25	5.15	96	1.95	95	61	27	2.94	142	83 ^e	0.283	2.75	3.27	22	3	
	1	5.39	110	2.54	109	44	32	1.77	126	81 ^e						
	7	3.14	64 ^e	2.42	104	56	42 ^e	2.47	97	61 ^e						
	18	4.86	101	3.22	137 ^e	52	40 ^e	1.88	89	57 ^e						
39	19										0.124	5.43	6.18	19		
	9	6.06	106	2.86	121 ^e	62 ^e	32	1.31	133	74 ^e						
Mean value for 16 normal subjects											0.219	1.86	2.04	20	3	

^aFunctional Residual Capacity/Total Lung Capacity.^bResidual Volume/Total Lung Capacity.^cIn liters/min at ambient pressure saturated with water vapor.^dAt most recent examination.^eSignificant difference from predicted value.

course of the study period in the three who could be followed. The investigators concluded that the exposed individuals suffered some fibrotic narrowing of bronchi and bronchioles, secondary to various degrees of bronchiolitis fibrosa obliterans.

Multiple clinical symptoms and biochemical and hematologic changes were described in workers engaged in the manufacture of sulfuric acid and hence exposed to an average of 4.9 mg/m^3 (2.6 ppm) NO_2 for 3 to 5 years (91). Because the data are not supported by diagnostic criteria, however, this report cannot be properly evaluated. Italian workers employed in the manufacture of nitric acid and exposed to an average of 56.4 to 65.8 mg/m^3 (30 to 35 ppm) NO_2 for an unspecified number of years exhibited no signs or symptoms of injury (92).

D. OTHER OXIDES OF NITROGEN

Although several other oxides of nitrogen besides NO and NO_2 exist in the atmosphere, they are generally present in very small quantities and except for nitrous oxide (N_2O) have not been of toxicological interest. Information concerning their effects is scarce.

Considerable attention has been focused on N_2O for the past century because of its anesthetic and analgesic properties. At concentrations of 80 percent ($1.44 \times 10^6 \text{ mg/m}^3$), N_2O is an effective general anesthetic. Inhalation of 10 to 20 percent N_2O (1.8×10^5 to $3.6 \times 10^5 \text{ mg/m}^3$) provides effective analgesia (93). Although extensive information relevant to these properties of N_2O is available, its inclusion is beyond the scope of this review.

E. FUTURE RESEARCH

Long term toxicological studies at more realistic ambient air

concentrations of NO_x (0.09 to 0.19 mg/m^3) are needed. Large animals, including primates, should be included in such studies. Studies employing an intermittent exposure regimen with daily peaks and studies in which the effect of exposure to a constant dose can be compared to exposure to periodic peaks are needed. More specifically, future research should include:

1. Further delineation of in vivo biochemical and biophysical effects of nitrogen oxide exposures relative to: 1. oxidation of fatty acid double bonds in cellular lipids and in lung surfactants; and 2. denaturation or alteration of lung proteins (collagen and elastin, enzymes, and cellular membranes).

2. Definition of the relationship of metabolic tissue changes to NO_2 dosage in terms of a concentration-time response. The relative importance of low-concentration, long-term exposures versus short-term peak concentrations should be studied.

3. Determination of the interaction of NO_x with other respiratory tract irritants (e.g. tobacco smoke, SO_2 , and infectious agents) in terms of biochemical, biophysical, infectious, and ultrastructural responses.

4. Assessment of the biologic importance of tolerance and cross tolerance in relation to other oxidant pollutants.

5. Determination of the effects of NO_2 on infectious disease defense mechanisms, immunological processes, and other hematological functions.

6. Continued evaluation of industrial exposure data.

F. SUMMARY

The two oxides of nitrogen present in ambient air in greatest quantities, nitric oxide (NO) and nitrogen dioxide (NO_2), are potential health hazards. Summaries of laboratory studies of animal exposures

are given in Tables 8-8, 8-9, and 8-10. Nitrous oxide is analgesic at concentrations of about 1.8×10^5 to 3.6×10^5 mg/m³ (1.0 to 2.0×10^5 ppm) and is a general anesthetic at concentrations of 1.4×10^6 mg/m³ (8.0×10^6 ppm) and above. Nitrogen oxides other than NO_x do not appear to be air pollution problems from a toxicological viewpoint at this time.

Nitric Oxide

At concentrations found in the atmosphere, NO is not an irritant and not considered to have adverse health effects. Its main toxic potential at ambient concentrations results from its oxidation to NO₂. A 12-minute exposure to 3075 mg/m³ (2500 ppm) NO was lethal to mice. Lower doses, from 24.6 mg/m³ (20 ppm) to 1.23×10^4 mg/m³ (10⁴ ppm), of NO produced reversible inhibition of bacterial hydrogenase activity.

Nitrogen Dioxide

Animal Studies

Nitrogen dioxide exerts its primary toxic effect on the lungs. Most of the available information on its toxicity comes from studies with animals. Concentrations greater than 188 mg/m³ (100 ppm) are lethal to most animal species, and 90 percent of the deaths are caused by pulmonary edema. The mortality rate may be modified by varying the exposure dosage (concentration x time), the temperature, and the presence of other irritants.

Pulmonary function. Short-term exposures to nonlethal concentrations of NO₂ have produced transient changes in pulmonary function in animals and man. Guinea pigs have shown increasee pulmonary resistance,

Table 8-8. SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS OF NITRIC OXIDE IN ANIMALS AND BACTERIA

Species	Concentration		Length of Exposure	Effects	Comment	Reference
	ppm	mg/m ³				
<u>Proteus vulgaris</u>	20	24.6	10 min	Reversible inhibition of hydro- genase activity		12
Rats	10	12.3	1 and 9 days	NO-hemoglobin and NO-meth- emoglobin not found in blood	Methemoglobin not examined	10
Rats	10	12.3	1 hr	Over 50 percent increase in methemoglobin	No methemoglo- bin formed	9
Guinea pigs	16 and 50	19.7 and 61.5	4 hr	No effect on respiratory rates and tidal volumes		4
<u>Proteus vulgaris</u>	10,000	12,300	10 min	Irreversible inhibition of hydrogenase activity		12
Mice	2,500	3,075	6 to 7 min	Death within 12 min. Recovered if returned to clean air after 4- to 6-min exposure		3

Table 8-9. SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF SHORT-TERM NO₂ EXPOSURE

Species	Concentration		Exposure hr	Effects	Comment	Reference
	ppm	mg/m ³				
Rats	0.5	0.9	4	Lung: Degranulation in mast cell morphology	Possibly precedes onset of acute inflammatory re- action	29
Rats	1.0	1.9	1	Lung: Degranulation in mast cell morphology	Mostly reversible 24 hr after exposure	29
Rats	1.0	1.9	4	Lung: Lipid peroxidation	Delayed effect; maximum response 24 hr after exposure	24
Rabbits	1.0	1.9	1	Lung: Structural changes in collagen of animals sacrificed immediately after exposure; reduced in animals sacrificed 24 hr after exposure	Chemical changes suggest denaturation of structural protein only partially reversed	22
Mice	3.5	6.6	2	Enhanced susceptibility to respiratory infection demonstrated by increased mortality after challenge with <u>K. pneumoniae</u>	Threshold for significant effect 6.6 mg/m ³ (3.5 ppm) for 2 hr when challenged 1 hr after exposure	69

Table 8-9 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF SHORT-TERM NO₂ EXPOSURE

Species	Concentration		Exposure hr	Effects	Comment	Reference
	ppm	mg/m ³				
Mice	5.0	9.4	2	Increased mortality when infected with <i>K. pneumoniae</i> either before or after NO ₂ exposure; reduced bacterial clearance from lungs		66
Rats	5.0	9.4	0.25	Performance: Decreased swimming rate		59
Guinea pigs	5.2 to 13.0	9.8 to 24.4	2 to 4	Lung: Increased respiratory rates and decreased tidal volumes		4
Mice	7.7	14.5	6	20% decrease in voluntary running activity		4
Rats	10 to 15	18.8 to 28.2	1	Blood: Significant increase in methemoglobin		9
Monkeys	10	18.8	2	Lung: Respiratory rate unchanged; tidal volume decreased; septal breaks, alveolar expansion, and some large air vesicles with thin septal walls observed	Tidal volume re- turned to pre- exposure levels within 48 hr	17

Table 8-9 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF SHORT-TERM NO₂ EXPOSURE

Species	Concentration		Exposure hr	Effects	Comment	Reference
	ppm	mg/m ³				
Monkeys	15	28.2	2	Lung: Respiratory rate unchanged; tidal volume decreased; moderate in alveoli expansion, minimal septal wall thinning, patchy lymphocytic interstitial infiltration Kidney: Some tubular erosion Liver: Cell ballooning with clear cytoplasm and nuclear displacement; interstitial congestion	Tidal volume returned to pre-exposure levels within 48 hr	17
Rabbits	24	45.0	0.25	Urine: Nitrate and nitrite ions detected		61
Rabbits	25	47.0	3	Decreased interferon production and decreased resistance to viral infection		74

Table 8-9 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF SHORT-TERM NO₂ EXPOSURE

Species	Concentration		Exposure hr	Effects	Comment	Reference
	ppm	mg/m ³				
Monkeys	35 to 50	65.8 to 94.0	2	Lung: Marked increase in respiratory rate with marked decrease in tidal volume; large areas of total alveolar collapse, edema, and lymphocytic infiltration with other areas of alveolar expansion and septal wall thinning; bronchial inflammation, epithelial surface erosion, and loss of cilia. Heart: Interstitial fibrosis and edema Kidney: Glomerular-tuft swelling and intercellular lymphocytic infiltration Liver: Lymphocytic infiltration, congestion, and centrilobular necrosis	Change in pulmonary function persisted up to 72 hr	17

Table 8-9 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF SHORT-TERM NO₂ EXPOSURE

Species	Concentration		Exposure hr	Effects	Comment	Reference
	ppm	mg/m ³				
Guinea pigs	40.0	75.2	0.5 hr at 2 hr intervals totaling 4.5 hr	Enzyme systems: Increased O ₂ consumption-- liver, spleen, kidney; increased lactic dehydrogenase-- liver, kidney, serum; increased aldolase--liver, spleen, kidney, serum		65
Rats, guinea pigs rabbits	75 to 80 100	141.0 to 150.4 188.0	2	Lung: Inflammation of bronchiolar epithelium	Apparent recovery 2 wk after expo- sure	27
Hamsters	100	188.0	6	Lung: Epithelial proliferation in major bronchi and more distal respiratory tract; depressed mucopolysaccharide production, increased phospholipid production, and increased lysozymal enzyme content		38
Rats	100	188.0	1	Blood: Methemoglobin present	Disappeared 1 to 2 hr after return to clean air	62
Rabbits, guinea pigs	150	282.0	1	Blood: Methemoglobin present		

Table 8-10. SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF LONG-TERM NO₂ EXPOSURE

Species	Concentration		Exposure	Effects	Comment	Reference
	ppm	mg/m ³				
Rabbits	0.25	0.5	4 hr/day, 6 days	Lung: Structural changes in collagen	Still apparent 7 days after final exposure	23
Mice	0.5	0.9	6 to 24 hr/day, 3 to 12 mo	Lung: Pneumonitis; alveolar distension	Possibly emphysematous condition	40
Mice	0.5	0.9	6 to 24 hr/day, 7 days/wk, up to 12 mo	Enhanced susceptibility to respiratory infection as demonstrated by increased mortality after challenge with <u>K. pneumoniae</u>	Significant increase after 3 mo exposure 24 hr/day and 6 mo at 6 and 18 hr/day. After 12 mo, increase significant at 24 hr/day only	55
Rats	0.8	1.5	Continuous, lifetime	Tachypnea and some terminal bronchiolar hypertrophy		94
Rabbits	1.3	2.5	Continuous, 17 wk	Reduction in rate of weight gain; 2% increase in exposed versus 8% in controls		56
Rats, monkeys	2.0	3.8	Continuous, 3 wk	Blood: Polycythemia	Approximate doubling of red cell number with lesser increases in hematocrit and hemoglobin	45
Rabbits	2.0	3.8	4 days	Morphological changes in terminal bronchiolar epithelium		47

Table 8-10 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF LONG-TERM NO₂ EXPOSURE

Species	Concentration		Exposure	Effects	Comment	Reference
	ppm	mg/m ³				
Rats	2.0	3.8	Continuous, lifetime	Lung: Bronchiolar epithelial changes-loss of cilia and reduced cytoplasmic blebbing crystalloid inclusion bodies	Possibly pre-emphysematous lesion. Effect occasionally seen at 1.5 mg/m ³ (0.8 ppm)	41
Rabbits	3.0	5.6	Continuous, 15 wk	Loss in weight; exposed group showed 10% decrease, 11% increase in control group		56
Guinea pigs	5.0	9.4	4 or 7.5 hr/day, 5 days/wk, 5.5 mo	Lung: Formation of circulating substance-possibly lung antibody; no change in expiratory flow resistance	Amounts increased with length of exposure	18
Monkeys	5.0	9.4	Continuous, 2 mo	Lung: Increased respiratory rate and decreased tidal volume	Minute volume unchanged. One of three monkeys exposed to influenza virus 24 hr before NO ₂ died after 5 days	71
Monkeys	10.0	18.8	Continuous, 1 mo	Lung: Both respiratory rate and tidal volume increased	Minute volume increased. Three monkeys exposed to influenza virus 24 hr before NO ₂ died within 3 days	71

Table 8-10 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF LONG-TERM NO₂ EXPOSURE

Species	Concentration		Exposure	Effects	Comment	Reference
	ppm	mg/m ³				
Rats	10 to 25	18.8 to 47.0	Continuous, 4 to 12 mo	Lung: Voluminous emphysema-like lungs; distended and disrupted alveoli Blood: Polycythemia	Associated thoracic kyphosis and rib flaring	44
Rats	12.0	22.6	Continuous, 9 mo	Weight: Decrease in rate of gain; exposed 20% below controls		41, 42
Guinea pigs	15.0	28.2	Continuous, 1 yr	Lung: Formation of circulating substance-possibly lung antibody		18
Guinea pigs	15.0	28.2	10 wk	Enzyme systems: Increased O ₂ consumption-spleen, kidney; increased lactic dehydrogenase-lung, liver, kidney; increased aldolase-liver, spleen, kidney, serum		65
Guinea pigs, rabbits	15 to 20 25	28.0 to 37.6 47.0	2 hr/day, 5 day/wk, for 21 mo	Lung: Inflammation of bronchiolar epithelium	Apparent recovery 21 days after final exposure	27

Table 8-10 (Continued). SUMMARY OF STUDIES OF TOXICOLOGICAL EFFECTS IN ANIMALS OF LONG-TERM NO₂ EXPOSURE

Species	Concentration		Exposure	Effects	Comment	Reference
	ppm	mg/m ³				
Rats, rabbits	24.0	45.1	6 hr/day, 5 days/wk, for 43 days (rats) or 45 days (rabbits)	Blood: Methemoglobin formation; mean: rabbits, 2.8% and rats, 13.6%	Animals exposed to welding fumes, which contained 3,075 to 6,150 mg/m ³ (2.5-5.0 ppm) NO as well as other contaminants; methemoglobin disappeared during post-exposure period	63
Dogs	25 to 26	47.0 to 48.9	6 mo	Lung: Bullous emphysema or scattered small bullae; diffuse increase in collagen	Early lesions of pulmonary emphysema produced; inclusion of ferric oxide with the NO ₂ appeared to exert a protective effect	50, 51
Hamsters	50	94.0	10 wk	Lung: Increase in volume, with a return to normal 2 wk after cessation of the exposure; transitory epithelial proliferation in respiratory bronchioles	No histological evidence of emphysema	38

increased respiratory rates, and decreased tidal volumes after exposure to concentrations of 9.8 mg/m^3 (5.2 ppm) for 2 hours, and 24.4 mg/m^3 (13.0 ppm) for 1 hour. Pulmonary function returned to normal when animals were returned to clean air. Similar changes in pulmonary function were observed in squirrel monkeys exposed for 2 hours to 18.8 to 94.0 mg/m^3 (10 to 50 ppm) NO_2 and in other monkeys exposed continuously for 2 months to 9.4 mg/m^3 (5 ppm) NO_2 . Monkeys (*M. speciosa*) continuously breathing 3.8 or 16.9 mg/m^3 (2 or 9 ppm) NO_2 developed tachypnea that persisted almost 2 years.

Rats continuously exposed to 1.5 mg/m^3 (0.8 ppm) NO_2 showed a 20 percent increase in respiratory frequency throughout their lifetimes. Dogs exposed to 0.9 to 3.8 mg/m^3 (0.5 to 2.0 ppm) NO_2 plus $245 \text{ } \mu\text{g/m}^3$ (0.2 ppm) NO for 18 months, however, showed no signs of changes in pulmonary function.

Performance. Rats exposed to 9.4 mg/m^3 (5 ppm) NO_2 while engaged in an 80 m swimming test that required approximately 15 minutes to complete and that was repeated 3 times a week had a 25 percent decrease in performance in the 5th week of the study.

Metabolism. The structure of lung collagen and elastin was altered in rabbits exposed to 1.9 mg/m^3 (1 ppm) NO_2 for 1 to 4 hours, but the lungs reverted to normal within 24 hours. Similar changes were observed in rabbits exposed to $470 \text{ } \mu\text{g/m}^3$ (0.25 ppm) NO_2 , 4 hours a day, for 6 days, but recovery was delayed and some damage persisted after 7 days. It has been suggested that the metabolic activity of lung tissue is reduced following exposure to NO_2 , and that repeated exposure,

with associated denaturation of collagen and elastin, may be a factor in the pathogenesis of pulmonary emphysema.

Lung lipids extracted from rats exposed to 1.9 mg/m^3 (1 ppm) NO_2 for 4 hours were peroxidated. The process was delayed and sustained - reaching a maximum at 24 hours after exposure - and was maintained for an additional 24 hours. Rats fed a vitamin-E-deficient diet and exposed to NO_2 had more peroxidation of surfactant and tissue lipids than similarly exposed rats receiving vitamin E supplementation.

Pathology. Pathological lesions have been observed in the lungs of animals following both short- and long-term NO_2 exposures. When exposed to 141 to 188 mg/m^3 (75 to 100 ppm) for 2 hours, rabbits, rats, and guinea pigs developed acute inflammation in bronchiolar epithelium, but appeared to recover 2 weeks after exposure. At 1.9 mg/m^3 (1 ppm) for 1 hour, or $940 \text{ } \mu\text{g/m}^3$ (0.5 ppm) for 4 hours, mast cells of rat lungs became degranulated, possibly signifying the onset of an acute inflammatory reaction. These cells returned to normal 24 hours after the end of exposure. More serious damage was found in lungs of squirrel monkeys exposed for 2 hours to 18.8 to 94.0 mg/m^3 (10 to 50 ppm) NO_2 ; primary lesions found at low concentrations turned into progressive alveolar expansion. Hyperplasia of the respiratory bronchiolar epithelium was seen in hamsters exposed to 84.6 to 103 mg/m^3 (45 to 55 ppm) for 10 weeks. A similar response was noted in the major bronchi and distal portions of the respiratory tract in hamsters exposed to 188 mg/m^3 (100 ppm) for 6 hours. Swelling of collagen fibrils was found in rats exposed to 320 mg/m^3 (17 ppm) NO_2 after exposure for 2 to 3 months with intermittent periods for recovery.

Chronic Changes. Since certain pathological changes seen in animals after experimental NO_2 exposure are similar to changes occurring in the pathogenesis of chronic obstructive pulmonary disease in man, it is suggested that long-term, low-level exposures to this pollutant may play a significant role in the development of chronic lung disease.

Improved histochemical and electron microscopic techniques have shown that long-term exposure of rats to NO_2 at concentrations that do not produce acute inflammatory responses have a cumulative and sustained effect. Emphysema-like lesions were produced in lungs of rats exposed to concentrations of 18.8 to 47.0 mg/m^3 (10 to 25 ppm). Rats exposed to 3.8 mg/m^3 (2 ppm) for their natural lifetime had fewer cilia; less-than-normal bronchiolar epithelial blebbing; and crystalloid, rod-shaped, intracytoplasmic inclusion bodies in their bronchiolar epithelium. Similar effects have been seen occasionally in rats continuously exposed to 1.5 mg/m^3 (0.8 ppm). Mice exposed to 940 $\mu\text{g/m}^3$ (0.5 ppm) for 3 to 12 months on 6-, 18-, and 24-hour daily schedules showed increases in the size of alveoli, resulting from alveolar distension rather than septal breakage. Additionally, inflammation of the bronchiolar epithelium with a reduction in distal airway size suggested the development of early focal emphysema. Rats exposed chronically to 18.8 to 47.0 mg/m^3 (10 to 25 ppm) NO_2 were observed to develop compensatory changes such as polycythemia, thoracic kyphosis, and a lateral flaring of the ribs. Early evidence of pulmonary emphysema was observed in dogs exposed continuously to 47.0 mg/m^3 (25 ppm) NO_2 for 6 months.

Susceptibility to Infection. Exposure of mice, hamsters, and squirrel monkeys to NO₂ causes increased susceptibility to bacterial pneumonia and influenza infections, as demonstrated by increased mortality, decreased survival time, and a reduction in ability to clear infectious agents from the lungs.

In mice, the threshold of increased susceptibility to Klebsiella pneumoniae occurred at 6.6 mg/m³ (3.5 ppm) NO₂ for 2 hours, if the infectious challenge was given within 1 hour after the NO₂ exposure. Mice infected with K. pneumoniae and exposed up to 72 hours later to 9.4 or 47.0 mg/m³ (5 or 25 ppm) NO₂ for 2 hours exhibited similarly enhanced susceptibility to the respiratory infection. Squirrel monkeys exposed to 18.8 mg/m³ (10 ppm) NO₂ for 2 hours and then challenged with K. pneumoniae aerosol retained the infectious agent in the lungs for extended periods of time. A 2-hour exposure to 94.0 mg/m³ (50 ppm) NO₂, followed by infectious challenge, led to markedly increased mortality in squirrel monkeys.

Continuous exposure reduces the NO₂ threshold concentration. In long-term studies of mice, significantly increased susceptibility to infection occurred after continuous daily exposure to 940 µg/m³ (0.5 ppm) NO₂ for 3 months, or after 6- or 18-hour daily exposure for 6 months. A significant increase in susceptibility to influenza virus or K. pneumoniae has also been found in squirrel monkeys continuously exposed to 18.8 and 9.4 mg/m³ (10 and 5 ppm) NO₂ for 1 and 2 months, respectively.

Impairment of interferon formation and decreased resistance to viral infection was demonstrated in rabbits exposed to 47.0 mg/m³ (25 ppm) NO₂ for a 3-hour period.

Systemic effects. Inhalation of NO_2 can produce systemic effects generally secondary to effects on the lungs. Monkeys exposed to 28.2 to 94.0 mg/m^3 (15 to 50 ppm) NO_2 for 2 hours exhibited cellular changes in heart, liver, and kidney tissue. Long-term exposure of rats to 2.5 to 5.6 mg/m^3 (1.3 to 3.0 ppm) for 15 to 17 months was associated with loss of weight and reduced rates of weight gain.

A circulating substance, possibly a lung antibody, was detected in the blood of guinea pigs exposed to 9.4 mg/m^3 (5.0 ppm) for 4 hours daily, 5 days per week, for 5.5 months. Guinea pigs exposed to 28.2 mg/m^3 (15 ppm) NO_2 for 10 weeks showed an alteration in O_2 consumption and enzyme activities (aldolase and lactic dehydrogenase) in the serum, lung, kidney, liver, and spleen. Rats and monkeys continuously exposed to 3.8 mg/m^3 (2.0 ppm) NO_2 for 3 weeks exhibited marked polycythemia. An increase in circulating methemoglobin was detected in the blood of several species exposed to concentrations greater than 122 mg/m^3 (70 ppm) NO_2 for 1 hour.

Human Studies

The small amount of information available concerning the toxicological effects of the oxides of nitrogen in man pertains to levels of these compounds higher than those normally found in ambient air. Experimental exposure of volunteer subjects to 9.4 mg/m^3 (5 ppm) NO_2 for 10 minutes produced a substantial, but transient, increase in airway resistance. Other information derived from occupational exposures to higher concentrations of NO/NO_2 mixtures is complicated in that other pollutants were present. Impaired pulmonary function, indicated by reduced maximal

breathing capacity, increased expiratory resistance, and occasional decreased vital capacity, was observed in patients accidentally exposed to high concentrations of nitrous fumes for a few minutes. In some cases, the impairment lasted for more than 2 years after the incident. Occupational exposure to 169 mg/m^3 (90 ppm) NO_2 for 30 minutes produced pulmonary edema and decreased vital capacity 18 hours later. Exposure to very high concentrations for about 5 minutes produced death within 2 days to 5 weeks.

The human threshold for perceiving the odor of NO_2 appears to be about $225 \text{ } \mu\text{g/m}^3$ (0.12 ppm).

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CHAPTER 9.

EPIDEMIOLOGICAL APPRAISAL OF NITROGEN OXIDES

A. INTRODUCTION

In contrast to the large volume of toxicological data, epidemiological data on the effects of exposure to nitrogen oxides (NO_x) are meager. Epidemiological studies have been primarily concerned with NO_2 because it is the oxide of nitrogen that has been most closely associated with effects on health. Generalizations drawn from the toxicological data in Chapter 8 form the basis for several of the epidemiologic studies presented in this chapter; that is, NO_2 is known to exert its primary toxic effect on the lungs and, in animals, exposure to NO_2 has been observed to be associated with increased susceptibility to respiratory infection and emphysematous changes.

Concomitant exposure to other pollutants, such as ozone, sulfur dioxide, metal fumes, and aerosols, presents a major problem in the interpretation of all information collected. The studies reported here have incorporated some measures to minimize interference by these factors.

B. EPIDEMIOLOGIC EVIDENCE OF LONG-TERM EFFECTS

1. The Cleveland Clinic Study - An Accidental High Exposure

On May 15, 1929, the X-ray room of the Cleveland Clinic (Cleveland, Ohio, U.S.A.) was engulfed in flames, 50,000 nitrocellulose films were ignited, and three explosions occurred (1). The air was filled with concentrations of nitric oxide (NO), carbon monoxide (CO), and hydrocyanic acid (HCN) estimated at 63.3 g/m^3 (51,500 ppm), 45.9 g/m^3

(40,000 ppm), and 6 g/m^3 (5,400 ppm), respectively. Ninety-seven individuals succumbed within 2 hours from the effects of CO and HCN. Neither CO nor HCN was considered the primary cause of death in the 26 additional individuals who died in less than 1 month, nor were either CO or HCN implicated in 92 nonfatal cases of serious physical injury. These effects were almost entirely attributed to oxides of nitrogen.

Much later, an epidemiological study was conducted to determine whether survivors of the disaster incurred a risk of dying sooner than nonexposed individuals.

Study groups consisted of individuals who:

1. Were present in the building at the time of the explosion.
2. Entered the building that afternoon.
3. Were exposed to smoke in an adjacent building.
4. Assisted rescue and first-aid workers.

An estimated 98 to 99 percent of the individuals present at the fire were enumerated by searching records and 87 percent of these were actually studied. Individuals who were present at the fire but who were not in any of the four exposure groups were used as controls.

When cumulative observed survival rates and cumulative expected survival rates were compared, their ratios, calculated for the years 1929 to 1965, showed no statistically significant differences between mortality rates of exposed and nonexposed groups.

2. The Chattanooga Studies - Ambient NO_2 and Respiratory Illness
 - a. Community effects

Shy et al. (2,3) studied the effects of community exposure

to NO₂ in four residential areas in greater Chattanooga, Tennessee, U.S.A. One area, in close proximity to a large trinitrotoluene (TNT) plant, had high-NO₂ and low-particulate pollution. Another had high-suspended particulate and low-NO₂ pollution. The two other areas served as "clean" controls.

Twenty-four-hour ambient air concentrations of total suspended particulate matter, suspended nitrates, suspended sulfates, and gaseous nitrogen dioxide were measured daily at each site in November 1968 and November 1969. From December 1968 through February 1969 and again in April 1969, these 24-hour concentrations were measured once every 4 days on a systematic sampling schedule. Twenty-four-hour ambient sulfur dioxide concentrations were measured once weekly in November 1968, but measurements were discontinued when concentrations were found to be less than 2.8 $\mu\text{g}/\text{m}^3$ (0.015 ppm) at each site.

Integrated 24-hour NO₂ samples were collected and analyzed by the Jacobs-Hochheiser method. Total suspended particulate matter, nitrate, and sulfate were collected with a high-volume sampler and subsequently analyzed.

Health-effects evaluation. Two possible health effects of NO₂ exposure were investigated in this community during the 1968-69 school year: 1) impaired ventilatory function in elementary school children and 2) increased frequency of acute respiratory illness in family groups. A total of 987 second-grade school children participated in the ventilatory testing. Weekly ventilatory function (forced

expiratory volume in 0.75 second, FEV_{0.75}) of each child was adjusted, by gender, for differences in individual standing height. These tests were made during November 1968 and March 1969. The second phase was a prospective study designed to assess the frequency of acute respiratory disease. A total of 4043 individuals in 871 families participated. At biweekly intervals from November 1968 through April 1969, each family was asked to report the incidence of new colds or sore throats, in terms of the age and sex of sick household members and the severity of the illness. Severity indices included the presence of fever, length of home confinement, and consultation with a doctor for treatment.

Area differences in respiratory illness rates were analyzed in the following groupings: the entire 24-week period, the influenza-A interval, the interim interval, and the influenza-B interval.

Conclusions. The ventilatory performance of second-grade school children in the high-NO₂ area was significantly less than that of children in the control areas.

In the high-NO₂ area and in the high-particulate area excess respiratory illness rates occurred in all family segments: second-grade children, siblings, fathers, and mothers. The relative excess was 18.8 percent in the high-NO₂ area and 10.4 percent in the high-particulate area. Area differences in illness rates could not be explained by differences in family composition, economic level, demographic characteristics, or prevalence of chronic conditions. Parental smoking habits did not appear to influence respiratory illness rates in second-grade children. Exposure to NO₂ and to

suspended particulates appear to be the most probable explanation for the observed excess in respiratory illness rates for the population. Severity of illness was essentially the same among all the areas; however, a precise NO_2 dose-response relationship could not be established from the data.

b. Acute Lower Respiratory Illness in Children

Later, Pearlman et al. (4) made a retrospective study of acute lower respiratory illness among infant cohorts and first and second graders living in three of the Chattanooga neighborhoods previously described (high-particulate area not included). Pearlman believed, on the basis of aerometric observations, that one of the control areas (Control 1) used in the Shy study could properly be designated an intermediate- NO_2 pollution area. The high- NO_2 pollution area and the other control area (Control 2) completed the pollutant-dose gradient for the Pearlman study.

Parents were asked to complete a questionnaire for the study children, reporting the frequency with which a physician had diagnosed croup, bronchitis, pneumonia, and asthma during the 3-year period from July 1966 through June 1969. Completed questionnaires were returned for 95 percent of the 1820 school children and 84 percent of the 1311 infants still residing in the study areas. Questionnaire responses were validated by physicians' office and hospital records. Sensitivity and specificity exceeded 67 percent for each clinical diagnosis.

Exposure to intermediate and high levels of NO_2 was associated with a significant increase in acute bronchitis among the infant

cohort, who were exposed for 3 years, and the school children who were exposed for 2 and 3 years.

Pearlman suggested a threshold relationship between NO_2 exposure and bronchitis, since the morbidity excess followed the pollutant gradient only among school children exposed for 3 years. Area differences in total acute lower respiratory illness could be accounted for by bronchitis excess. Croup, pneumonia, and hospitalizations for acute lower respiratory illness did not show significant area differences.

Since the high- NO_2 pollution area of this study included a school area exposed to NO_2 levels about the same as the levels in the intermediate area, the difference in NO_2 exposure levels between the high and intermediate areas was diminished. This may explain why the illness rates of some intermediate exposure groups exceeded the rates of high exposure groups. Groups within each school of the high- NO_2 area were too small, however, to allow separate analysis of illness rates.

The Pearlman study corroborated Shy's observation that excess acute respiratory illness can be found among children living in NO_2 -polluted areas. He suggested that acute lower-respiratory illness may be a more selective, sensitive indicator of pollutant effect upon host response than is acute general respiratory illness.

The Chattanooga study was recently re-evaluated by EPA personnel because of problems associated with the aerometric measurement system used in the study. This re-evaluation (5) concludes that an

annual average concentration of about $150 \mu\text{g}/\text{m}^3$ (0.08 ppm) of NO_2 was associated with adverse health effects in Chattanooga.

3. Czechoslovakian Study - Effects of Ambient NO_2 and SO_2 on Peripheral Blood

Studies by Petr and Schmidt (6) of Czechoslovakian children who lived near a factory that emits NO_x and SO_2 have produced some positive information. Data are available from three towns.

1. Ohrozenice, which experiences air pollution that is predominately SO_2 [concentrations ranging from 30 to $320 \mu\text{g}/\text{m}^3$ (0.01 to 0.12 ppm)], with slight admixtures of NO_x [concentrations ranging from 5 to $50 \mu\text{g}/\text{m}^3$ *].

2. Rosice, which experiences a larger amount of NO_x pollution (concentrations ranging from 20 to $70 \mu\text{g}/\text{m}^3$) and only a small amount of SO_2 pollution [concentrations up to $12 \mu\text{g}/\text{m}^3$ (0.005 ppm)].

3. Bohdanec, which has no nearby air pollution sources.

Petr and Schmidt (6) observed a statistically significant difference in the configuration of lymphocytes and monocytes in the smears of peripheral blood from children in the three areas. Although they failed to indicate the size of the study group, they noted that the children did not differ from one another in age or socioeconomic grouping. The investigators consider the results to be a sensitive indicator of the children's reaction to SO_2 and nitrous gases in the environment.

*It is not possible to calculate ppm from total oxides of nitrogen.

When they studied the blood of ten 8- to 10-year-old children from each of the three towns, Petr and Schmidt (6) observed relative increases in resistance to hemolysis and increases in number of immature red blood cells in children from Rosice (high- NO_2 , low- SO_2) and Ohrazenice (high- SO_2 , low- NO_2) as compared to children from Bohdanec (control). They interpreted this as a compensatory response of the children to noxious substances in the environment. Methemoglobin levels were determined in these same children, and the investigators observed an average of 2.5 percent methemoglobin in the blood of the Rosice (high- NO_2 , low- SO_2) children, compared to an average of 0.86 percent in the children from Bohdanec (control). The difference was statistically significant ($p < 0.025$), but the possible contribution of large amounts of nitrates in the drinking water could not be overlooked. When the study was repeated in the Rosice (high- NO_2 , low- SO_2) children at a later date, after the source of atmospheric nitrous gases had been controlled, they found no abnormal levels of methemoglobin. The authors implicated the atmospheric NO_x as an etiologic agent in the observed methemoglobinemia.

It is difficult to interpret the significance of hematological changes. More experimental and epidemiological work is needed to confirm these data. For example, no information is given about antecedent viral or bacterial infections, which are known to infect children seasonally and could explain peripheral blood changes. Controlled studies of red-cell age, and of lymphocyte and monocyte morphology are also needed.

4. Occupational Exposure

While occupational exposures to NO_x are fairly common, either in connection with the use of rocket fuel (nitrogen tetroxide) or dynamite, most occupational exposures are to mixed pollutants and many are poorly documented. Among the frequently cited studies are those of Vigdortschik (7), who presented evidence that nitrogen oxide exposure over many years is capable of producing pulmonary fibrosis; and of McCord (8), who suggested that some methemoglobinemias occur as a result of nitrogen oxide exposure among welders. Such studies, although suggestive, need further confirmation.

C. FUTURE RESEARCH

The dearth of information relating community health effects to ambient concentration of NO_x is apparent, but the following studies are particularly needed:

1. Studies to determine which segment of the population is most susceptible to abnormal levels of NO_x .

2. Studies to delineate precisely the relationship among methemoglobin levels, peripheral blood alterations, and NO_x concentrations.

3. Replication of studies of the enhanced susceptibility to respiratory infection at various NO_x levels.

4. Studies to determine the relationship of other pollutants to the oxides of nitrogen and their combined effect on human health.

D. SUMMARY

There is a paucity of well-controlled epidemiological studies involving exposure of human populations to ambient levels of nitrogen

oxides. The Cleveland Clinic Fire of 1929 exposed many employees to extremely high levels of HCN, CO, and NO_x. A follow-up study of survivors revealed no increase in mortality in the exposed employees over the control employees.

Effects of community exposure to NO₂ in four residential areas of greater Chattanooga were studied. In one area, NO₂ concentrations were high and particulate matter was low; in another, NO₂ concentrations were low and particulate matter was high. Two other areas served as "clean" controls.

The ventilatory performance (FEV_{0.75}) of children in the high-NO₂ area was significantly reduced when compared to the performance of children in the control areas. In addition, an 18.8 percent relative excess of respiratory illness occurred among families living in the elevated-NO₂ area.

In a retrospective study of the same Chattanooga area, exposure to intermediate and high levels of NO₂ in ambient air was associated with a significant increase in the frequency of acute bronchitis.

The effects noted in these studies are associated with an annual exposure to about 150 µg/m³ (0.08 ppm) of NO₂.

A report from Czechoslovakia indicates that NO_x produced several alterations in the peripheral blood. Increased levels of methemoglobin were observed in school children residing in a town that had relatively high ambient levels of NO_x; however, the findings of this report require further, clarifying investigation.

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APPENDIX.
VOLUME TO MASS CONVERSION TABLES

VOLUME (ppm) TO MASS ($\mu\text{g}/\text{m}^3$) CONVERSION TABLE FOR NO
 (ppm $\times 1230 = \mu\text{g}/\text{m}^3$ at 25° C, 760 mm Hg)

ppm	$\mu\text{g}/\text{m}^3$	ppm	$\mu\text{g}/\text{m}^3$	ppm	$\mu\text{g}/\text{m}^3$
0.01	10	0.36	440	0.71	870
0.02	20	0.37	460	0.72	890
0.03	40	0.38	470	0.73	900
0.04	50	0.39	480	0.74	910
0.05	60	0.40	490	0.75	920
0.06	70	0.41	500	0.76	930
0.07	90	0.42	520	0.77	950
0.08	100	0.43	530	0.78	960
0.09	110	0.44	540	0.79	970
0.10	120	0.45	550	0.80	980
0.11	140	0.46	570	0.81	1000
0.12	150	0.47	580	0.82	1010
0.13	160	0.48	590	0.83	1020
0.14	170	0.49	600	0.84	1030
0.15	180	0.50	620	0.85	1050
0.16	200	0.51	630	0.86	1060
0.17	210	0.52	640	0.87	1070
0.18	220	0.53	650	0.88	1080
0.19	230	0.54	660	0.89	1090
0.20	250	0.55	680	0.90	1110
0.21	260	0.56	690	0.91	1120
0.22	270	0.57	700	0.92	1130
0.23	280	0.58	710	0.93	1140
0.24	300	0.59	730	0.94	1160
0.25	310	0.60	740	0.95	1170
0.26	320	0.61	750	0.96	1180
0.27	330	0.62	760	0.97	1190
0.28	340	0.63	770	0.98	1210
0.29	360	0.64	790	0.99	1220
0.30	370	0.65	800	1.00	1230
0.31	380	0.66	810		
0.32	390	0.67	820		
0.33	410	0.68	840		
0.34	420	0.69	850		
0.35	430	0.70	860		

VOLUME (ppm) TO MASS ($\mu\text{g}/\text{m}^3$) CONVERSION TABLE FOR NO_2
 (ppm x 1880 = $\mu\text{g}/\text{m}^3$ at 25° C, 760 mm Hg)

ppm	$\mu\text{g}/\text{m}^3$	ppm	$\mu\text{g}/\text{m}^3$	ppm	$\mu\text{g}/\text{m}^3$
0.01	20	0.36	680	0.71	1330
0.02	40	0.37	700	0.72	1350
0.03	60	0.38	710	0.73	1370
0.04	80	0.39	730	0.74	1390
0.05	90	0.40	750	0.75	1410
0.06	110	0.41	770	0.76	1430
0.07	130	0.42	790	0.77	1450
0.08	150	0.43	810	0.78	1470
0.09	170	0.44	830	0.79	1490
0.10	190	0.45	850	0.80	1500
0.11	210	0.46	860	0.81	1520
0.12	230	0.47	880	0.82	1540
0.13	240	0.48	900	0.83	1560
0.14	260	0.49	920	0.84	1580
0.15	280	0.50	940	0.85	1600
0.16	300	0.51	960	0.86	1620
0.17	320	0.52	980	0.87	1640
0.18	340	0.53	1000	0.88	1650
0.19	360	0.54	1020	0.89	1670
0.20	380	0.55	1030	0.90	1690
0.21	390	0.56	1050	0.91	1710
0.22	410	0.57	1070	0.92	1730
0.23	430	0.58	1090	0.93	1750
0.24	450	0.59	1110	0.94	1770
0.25	470	0.60	1130	0.95	1790
0.26	490	0.61	1150	0.96	1800
0.27	510	0.62	1170	0.97	1820
0.28	530	0.63	1180	0.98	1840
0.29	550	0.64	1200	0.99	1860
0.30	560	0.65	1220	1.00	1880
0.31	580	0.66	1240		
0.32	600	0.67	1260		
0.33	620	0.68	1280		
0.34	640	0.69	1300		
0.35	660	0.70	1320		